

**Diastereoselective Synthesis of Planar Chiral *N*-Substituted Ferrocenes
Derived from Epimeric Imidazolones and their Application to Asymmetric
Hydrogenation of Quinolines**

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To my family

Abstract

This thesis describes the synthesis and use of an *N*-substituted ferrocene bearing a proline-derived chiral directing group and diastereoselective lithiation-electrophile quench of the pro- S_p hydrogen of the ferrocene to give planar chiral products in >95:5 dr. The auxiliary group is found to be stable to lithium bases of types RLi and R_2NLi giving the same diastereoselectivity. The *anti*- epimer of the previously mentioned *syn* auxiliary induces lithiation of pro R_p rather than pro S_p hydrogen in >95:5 dr. Upon electrophile quench and elimination, the enantiomer of the *syn*-derived planar chiral imidazolone is obtained. Hence, this method provides a practical way to prepare planar chiral enantiomers in this series without the use of a more expensive D-proline derived starting material. The *syn* and *anti* epimers have β , γ -stereogenic centers and the origin of stereoselectivity in lithiation appears to be driven by the conformational bias exerted by the β -silyloxy moiety in each chiral auxiliary. In the thesis, this conclusion is supported using insensitivity of lithiation selectivity to the bulkiness of the base, comparison of enantiomers, deuteration experiments, nOe difference studies and computational modeling of the ground states and lithiation transition states for both substrates. The products are then converted to ligand precursors to make iridium and rhodium complexes. Among them, one of the cationic iridium complex is found to be effective in the asymmetric hydrogenation of 2-substituted quinolines with enantioselectivities up to 80% at pressures as low as 5 atm.

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Abbreviations

aq.	aqueous
BAr ^F	tetra[3,5-bis(trifluoromethylphenyl)]borate
Bu	butyl
CbzCl	benzyl chloroformate
cod	1,5-cyclooctadiene
conv.	conversion
Cp	cyclopentadienyl
CSP	chiral stationary phase
DMF	dimethyl formamide
de	distereomeric excess
dr	diastereomeric ratio
DIBAL-H	diisobutylaluminium hydride
DMPEG	poly(ethylene glycol)dimethyl ether
DPP	diphenyl phosphate
DPEN	diphenylethylene diamine
DTBM	3,5 di-tert-butyl 4-methoxy phenyl
ee	enantiomeric excess
equiv.	equivalents
er	enantiomeric ratio
E ⁺	electrophile
h	hours
HPLC	high pressure liquid chromatography

<i>I</i>	iso
IR	infrared
Ir	iridium
LDA	lithium diisopropylamide
LTMP	lithium 2,2,6,6-tetramethyl piperidine
min	min.
<i>n</i>	normal
NHC	<i>N</i> -heterocyclic carbene
NMR	nuclear magnetic resonance
<i>o</i>	ortho
<i>p</i>	para
quant.	quantitative
Ph	phenyl
Pr	propyl
rt	room temperature
Rh	rhodium
Ru	ruthenium
<i>s</i>	secondary
<i>t</i>	tertiary
TES	triethylsilyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography

TMS	trimethylsilyl
TMCD	<i>N,N,N',N'</i> -tetramethy-1,2-
	diaminocyclohexane
TOF	turn over frequency
TON	turn over number
TS	transition state

Introduction

Asymmetric synthesis has become a major aspect of modern organic chemistry. The stereochemical purity of an organic compound is crucial when dealing with biologically active pharmaceuticals and agrochemicals. Synthesis of an optically pure compound can be achieved by the use of enantiomerically pure starting material, resolution of a racemic mixture or by asymmetric catalysis. A good chiral auxiliary not only provides enantiomerically pure compounds but also enables its manipulation using simple reagents. Asymmetric catalysis is an important aspect of asymmetric synthesis, where stereocenters are established through the use of a chiral catalyst.

Metal-catalyzed reactions did not play a major role in many classic complex natural product syntheses such as Robinson's¹ 1917 tropinone synthesis to Eschenmoser² and Woodward's³ 1973 coenzyme B₁₂ synthesis. However modern organic syntheses often make use of numerous transition-metal catalyzed transformations. The use of catalytic reactions has grown in such a way that some of them, for example alkene metathesis, have no parallel in traditional organic chemistry. In some cases catalysis enhances the rate and generality considerably such as Buchwald-Hartwig amination of aryl halides, in some other cases it enhances selectivity, as in asymmetric hydrogenation. Asymmetric catalysts hence play a major role in the synthesis of enantiomerically pure drugs and agrochemicals by lowering the amount of "undesired" isomer.⁴ However, achieving high levels of stereoselectivity requires considerable innovation, and provides a practical challenge for chemists.

The first part of this dissertation will outline the synthesis of *N*-substituted planar chiral ferrocenes by diastereoselective lithiation-electrophile quench using an inexpensive

and readily available proline derived chiral directing group. This approach represents the first documented chiral auxiliary with nitrogen directly attached to the ferrocene ring. The use of this chiral auxiliary also allows the conversion of *ortho*-substituted products to solely planar chiral ferrocene derivatives. By use of simple reagents, complete manipulation of the directing group into primary amines and ligand precursors such as imidazolones will be described. The second part will outline the studies on the origin of stereochemistry in lithiation of this directing group based on experimental results and computational calculations. The presence of β,γ -stereogenic centers arises the question of whether the directing group is controlled by the Cp ring or base. The studies on the role of the β -silyloxy moiety in determining the origin of stereochemistry will be explained with the use of lithiation-substitution reactions of epimers and computational modelling of transition states of lithiation. The synthesis of either enantiomer of these compounds by changing one stereocenter in the chiral auxiliary becomes possible.

The final part will outline the use of products from these reactions to make unusual C_1 -symmetric ligands. Synthesis of cationic iridium complexes using these chiral ligands and their use in asymmetric hydrogenation will take the project to the application level. The final part of the thesis will discuss the asymmetric hydrogenation of recalcitrant 2-substituted quinolines under pressures as low as 5 atm. Finally, attempts towards improvements in the enantioselectivity of asymmetric hydrogenation of quinolines by incorporation of bidentate ligands will be presented.

1. Historical

1.1. Stereoselective Synthesis of Planar-Chiral Ferrocenes

1.1.1. Ferrocenes: Synthesis and Applications

Ferrocene, or *bis*(cyclopentadienyl)iron (**2**), was first reported independently by two groups. Kealy and Pauson published their contribution in *Nature*⁵ in 1951 while Miller, Tebboth and Tremaine reported preparation of the identical compound in the *Journal of the Chemical Society*.⁶ Both groups postulated the structure of ferrocene as having two cyclopentadienyl (Cp) rings individually sigma-bound to the Fe(II) centre **1**. Soon after publication of these reports, researchers took interest in these compounds and the correct ferrocene structure (**2**) and its aromaticity were published by Woodward & Wilkinson⁷ and Fischer & Pfab,⁸ as seen in Figure 1. These proposals were independently confirmed by X-ray structural analysis.⁹ For their elegant work on metallocenes, Wilkinson and Fischer were awarded Nobel Prize in 1973.

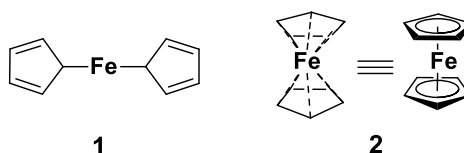
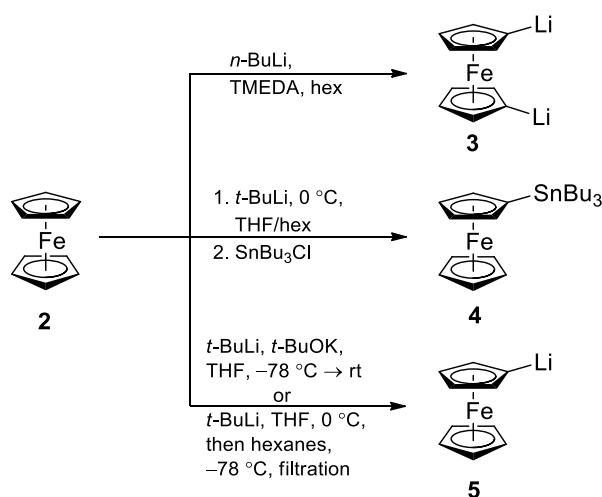


Figure 1. Structure of ferrocene.

Ferrocenes behave as electron-rich aromatics because of the partial negative charge of cyclopentadienyl ligands. These compounds undergo electrophilic aromatic substitution 3×10^6 times faster than benzene.¹⁰ The presence of oxidizing electrophiles causes decomposition of ferrocene, which prevents their use in electrophilic halogenation and nitration. Hence only radical and electrophilic substitution reactions such as Friedel-Crafts acylation, borylation (under non-oxidizing conditions), mercuration, and lithiation

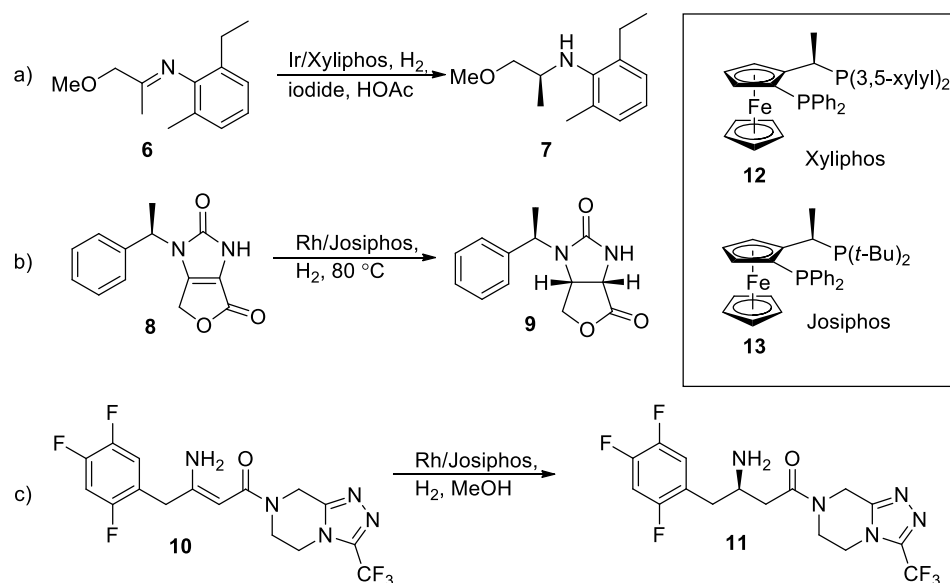
are used in the synthesis of substituted ferrocenes. Among them, incorporation of a heteroatom can be carried out using lithiation and mercuration.

Lithiation is the most convenient method for the preparation of ferrocene derivatives.¹¹ Lithiation with *n*-butyllithium yields mixtures of mono and 1,1'-dilithiated species though exclusive formation of dilithioferrocene **3** can be achieved by activating *n*-BuLi with *N,N,N',N'*-tetramethylethylenediamine (TMEDA) in hexane.¹² Kagan and coworkers carried out investigations on lithiating reagent, reaction time, temperature and solvent system to find the best lithiation conditions to get subsequent monosubstituted ferrocene derivatives.¹³ By their method, stannane **4** may be prepared on up to 20 g scale which only requires distillation for its purification. A more reliable preparation was reported by Bildstein whereby monolithioferrocene **5** can be isolated as a pyrophoric orange solid by Schlenk filtration and stored under cold conditions and inert atmosphere.¹⁴ Another way of obtaining good conversion to monolithioferrocene is using *t*-BuLi/*t*-BuOK which allows *in situ* quench to afford the monosubstituted product (Scheme 1).¹⁵



Scheme 1. Synthesis of mono and dilithioferrocenes.

Ferrocene as a ligand backbone offers more degrees of freedom and the different conformations of cyclopentadienyls enable the ligand to reduce steric strain. In addition to its unique structure, ferrocene has thermal stability and good tolerance to oxygen, moisture and many reagents. Owing to these unique properties, ferrocene derivatives have been used significantly in academia and industry as ligands for various transformations. The most well-known ferrocene ligand, [1,1'-bis(diphenylphosphino)ferrocene] (dppf) was first described in 1965.¹⁶ Another well-known ferrocenyl ligand is the Ir/Xyliphos catalyst **12** used for enantioselective imine hydrogenation (Scheme 2a). The intermediate obtained in the synthesis of the herbicide (*S*)-metolachlor is the largest scale known enantioselective catalytic process produced by Ciba-Geigy/Syngenta.¹⁷ The hydrogenation of a tetrasubstituted olefin in presence of Josiphos **13** was the key step for the synthesis of biotin by Lonza (Scheme 2b).^{17b} Merck chemists reported the hydrogenation of unprotected dehydro β -amino acid intermediate for MK-0431 catalyzed by Rh/Josiphos with ee up to 94% (Scheme 2c).¹⁸



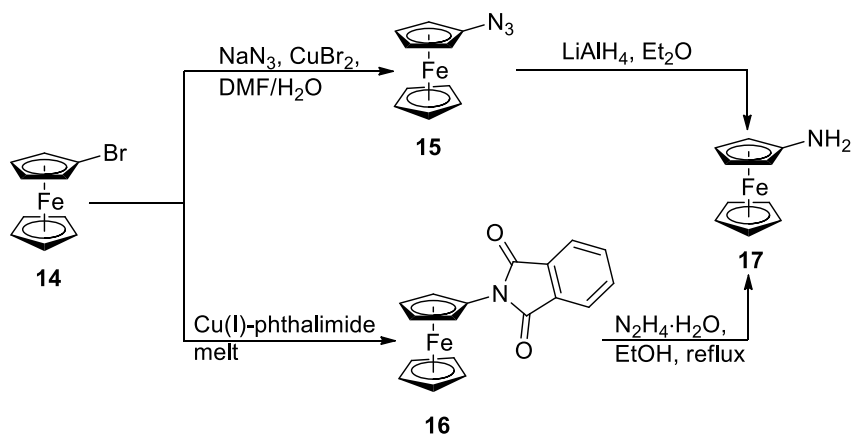
Scheme 2. Important industrial applications of ferrocenyl diphosphine ligands.

In addition to ferrocenyl ligands containing *P*-donors, *N*-, *S*-, *O*- substituted ligands are also used in various metal-catalyzed reactions such as hydrogenation and cross-coupling reactions. However, a reliable and versatile route to the synthesis of nitrogen substituted directly onto ferrocene cyclopentadienyl ring remains underexplored.¹⁹ This can be understood from the price of 1g of aminoferrocene - more than \$460!¹⁰ The lack of a good synthetic method for the synthesis of aminoferrocenes, in particular, planar chiral *N*-substituted ferrocenes has hampered the use of potential *N*-donor ferrocenyl ligands in various asymmetric metal-catalyzed reactions. This has facilitated the development of several synthetic routes towards the synthesis of aminoferrocene over the past 60 years.

1.1.2. Aminoferrocenes

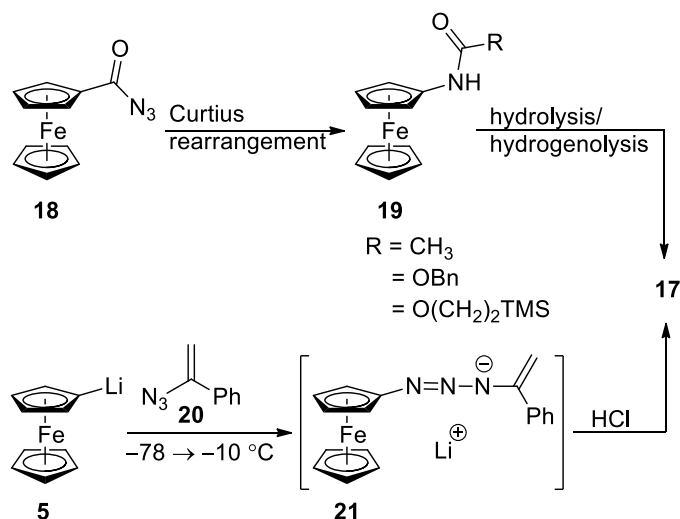
Aminoferrocene (**17**) was first synthesized by Arimoto²⁰ and Nesmeyanov²¹ independently in 1955. In Nesmeyanov's initial synthesis, FcLi was treated with *O*-benzyl ether of hydroxylamine to give **17**, in low yield. Later on, the same group reported two alternative routes towards aminoferrocene starting from bromoferrocene: (i) by reduction of azidoferrrocene synthesized by treating **14** with sodium azide under copper catalysis and (ii) by deprotection of *N*-ferrocenylphthalimide, **16** synthesized by heating bromoferrocene with copper phthalimide as a melt.²¹⁻²² A modification to the latter route was reported by Sato using iodoferrocene, Cu₂O and phthalimide to obtain **17** more conveniently.²³ On the basis of works from Sato and Nesmeyanov, a high yielding synthetic pathway employing iodoferrocene as starting material was reported by Bildstein¹⁴ which was later slightly modified by Heinze.²⁴ The synthesis involves

coupling of iodoferrocene with copper phthalimide to give ferrocenyl phthalimide which was converted to aminoferrocene using the Gabriel synthesis.



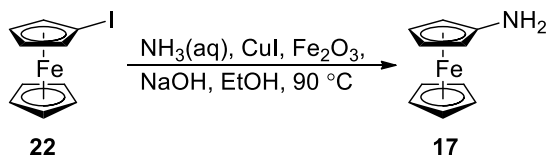
Scheme 3. Aminoferrocene synthesis using azide or phthalimide.

Arimoto's synthesis involved treatment of ferrocenecarboxylic acid with PCl_5 in benzene followed by NaN_3 in acetone to form ferrocenoyl azide **18**. Curtius rearrangement and subsequent removal of the benzyl formate group gave aminoferrocene. A similar strategy was employed by Herberhold and Butler which involves Curtius rearrangement of acyl azide and subsequent cleavage of corresponding amide²⁵ or carbamate.²⁶ Another convenient method for generation of **17** is by quenching lithioferrocene by azidostyrene **20** followed by acidic workup to convert intermediate **21** to aminoferrocene (Scheme 4).²⁷



Scheme 4. Preparation of aminoferrocene using acyl azide or azidostyrene.

A direct metal catalyzed coupling of iodoferrocene using liquid ammonia as the nitrogen source in presence of CuI/Fe₂O₃ cocatalyst system in ethanolic solution was recently reported, which gave **17** in 65% yield (Scheme 5).²⁸ Gasser and coworkers employed the same synthetic methodology for the synthesis of aminoruthenocene as well.



Scheme 5. Cu/Fe catalyzed synthesis of aminoferrocene using liquid ammonia.

1.1.3. Planar Chiral Ferrocenes

The planar chirality of ferrocenyl compounds substituted with different groups at positions 1 and 2 are due to loss of both σ_v plane of symmetry and inversion axis. The absolute configuration is assigned by looking along the C₅ axis of ferrocene with the more substituted ring directed towards the observer (Figure 2). When R₁ > R₂, the

compound has (*R*) planar chiral configuration; when $R_2 > R_1$, the compound has (*S*) planar chiral configuration.²⁹

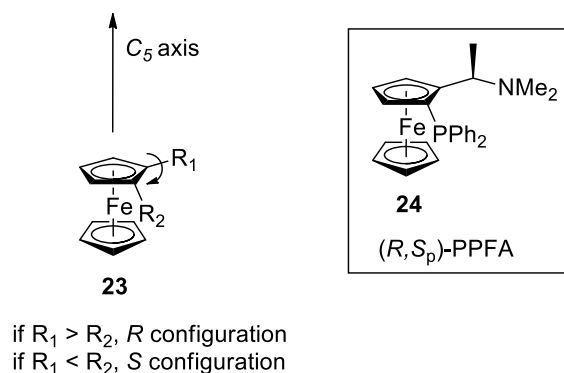


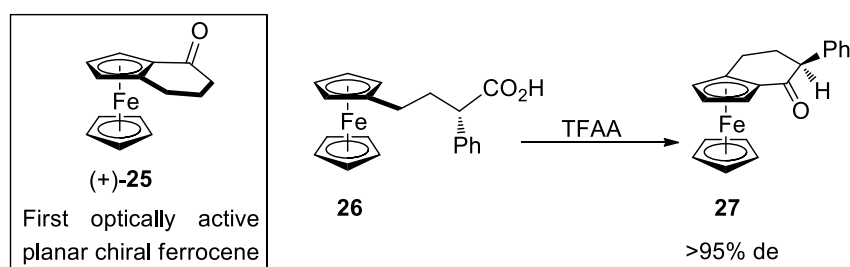
Figure 2. Assignment of planar chirality in ferrocenes.

As planar chirality differs from central chirality, the notations used are R_p and S_p instead of “(*R*)” and “(*S*)”. When ferrocenyl compounds have more than one type of chirality, the priority order of elements is central > axial > planar > helicity.³⁰

Soon after Woodward and co-workers classified ferrocene as an aromatic compound, researchers applied electrophilic substitution reactions to synthesize planar chiral ferrocenes.³¹ The major drawback of this approach was fairly low selectivity towards exclusive substitution of either α or β position. Even though the increase in steric bulk led to an increase in selectivity of monoacetylation of ethyl ferrocene as observed by Rosenblum and Woodward, the isolation of pure product required tedious work up and repeated recrystallizations.³²

Greater success was achieved by Thompson in 1959 when chemical resolution was used and thus the first optically active planar chiral ferrocene compound was synthesized. When **25** was treated with (–)-menthydrazone followed by acid mediated cleavage of hydrazine 8 mg of (+)-**25** was isolated.³³ The absolute configuration of this

compound was determined by Schlögl and coworkers using Horeau's method.³⁴ Later in 1965, the same group reported the synthesis of an (*S*, *S_p*) analogue of **25**, containing an α -phenyl group, derived from (*S*)- α -phenyl- γ -ferrocenylbutyric acid **26** in high diastereoselectivity (>95% de) (Scheme 6).³⁵ Over the years more efficient methods were developed which allowed easier access to planar chiral ferrocenes. However the lithiation-electrophile quench has proven to be an important tool which, in these cases, is used almost exclusively.³⁶

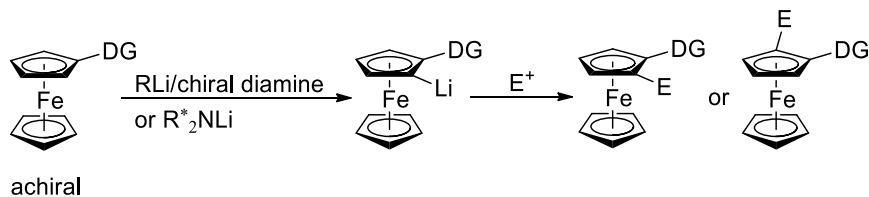


Scheme 6. Initial studies on the stereoselective synthesis of planar chiral ferrocenes.

In principle, the methods for the introduction of planar chirality onto ferrocene moiety can be classified into three types: (a) enantioselective lithiation-substitution (b) diastereoselective lithiation-substitution and (c) resolution of racemic planar chiral ferrocenes by enzymatic or non-enzymatic kinetic resolution.

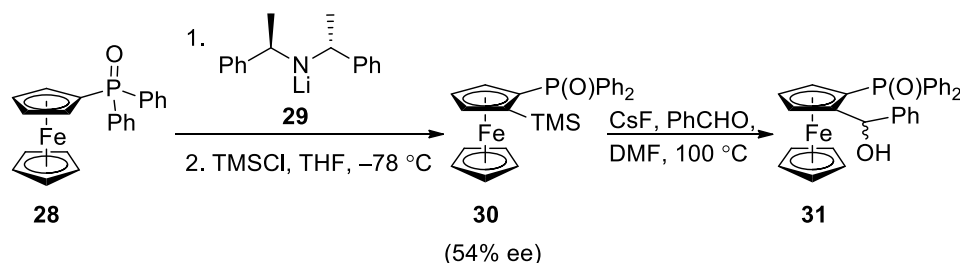
1.1.3.1. Enantioselective Synthesis of Planar Chiral Ferrocenes

In this method, mono-substituted ferrocenes with achiral directing groups are used in presence of chiral alkyllithium or lithium dialkyl amide bases to differentiate between the two prochiral *ortho*-positions on the Cp ring.



Scheme 7. Enantioselective lithiation-substitution.

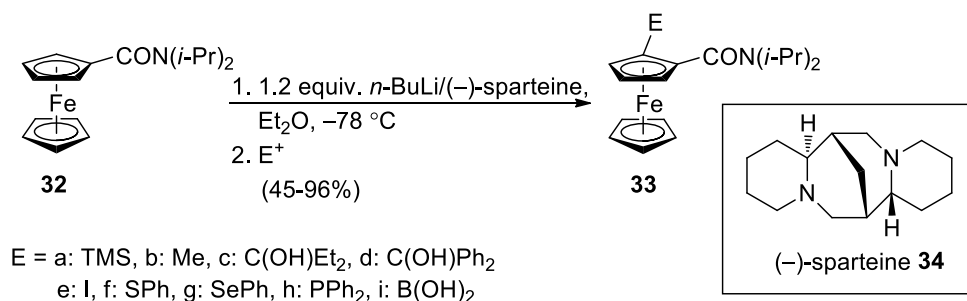
The initial attempts towards an enantioselective lithiation was reported in 1970 by Nozaki, where a (–)-sparteine (**34**)-mediated lithiation of isopropylferrocene afforded mixtures of products in low enantiomeric excess.³⁷ In 1995, Simpkins, based on their work on (η^6 -arene) chromium tricarbonyl complexes,³⁸ carried out *ortho* lithiation using a chiral LDA analogue called the Simpkins' base **29**.³⁹ Diphenylphosphine oxide **28** in the presence of chiral lithium amide base afforded *ortho*-substituted trimethylsilyl adduct **30** in moderate enantioselectivity (Scheme 8). Attempts at subjecting **30** to further metallation using alkyl lithium bases were fruitless, however, reaction with benzaldehyde in presence of CsF gave secondary alcohol **31** as a 1:1 mixture of diastereomers.



Scheme 8. Enantioselective lithiation using Simpkins' base.

A breakthrough in this area of chemistry occurred when Snieckus and coworkers reported the selective *ortho*-lithiation of *N,N*-diisopropyl ferrocenecarboxamide **32** in the presence of (–)-sparteine (**34**) to yield 1,2-disubstituted ferrocene products in excellent

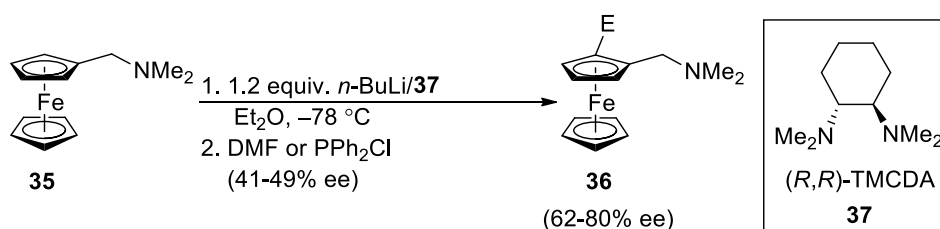
enantiomeric excess after electrophile quench (Scheme 9).⁴⁰ This work was based on the comprehensive work by Hoppe on the enantioselective synthesis using lithium/(-)-sparteine carbanion pairs.⁴¹



Scheme 9. (-)-sparteine-mediated *ortho*-lithiation using ferrocenyl carboxamide.

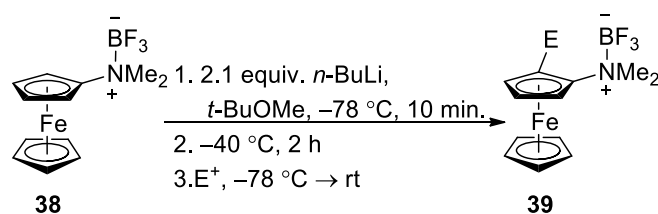
Using this method, carbon and heteroatom based substituents could be installed with ease and high enantioselectivity. When these products were subjected to subsequent lithiation, substitution at the lower Cp ring occurred to give 1,2,1'-trisubstituted product. An unprecedented slow racemization of ferrocene was observed during the reaction due to a substituted Cp-aryl ligand exchange by an unknown mechanism. Since the manipulation of the diisopropyl amide was difficult, enantioselective lithiation was extended to *N*-cumyl-*N*-ethylferrocenecarboxamide which gave the same yields and selectivities as the diisopropyl amide.⁴²

Uemura reported the use of *N,N,N',N'*-tetramethyl-(1*R*,2*R*)-cyclohexanediamine-[(*R,R*)-TMCD] mediated asymmetric lithiation of (dimethylaminomethyl)ferrocene **35** to give products up to 80% ee (Scheme 10). In this case, use of (-)-sparteine (**34**) gave unexpectedly poor results.⁴³



Scheme 10. Enantioselective lithiation of (dimethylaminomethyl)ferrocene.

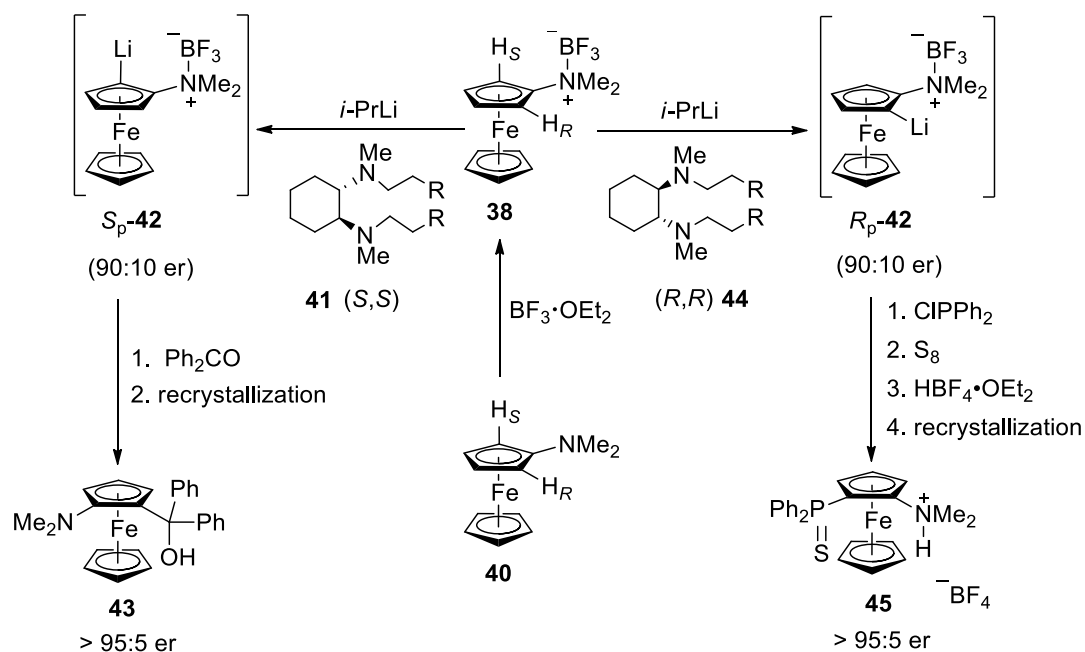
The first report on the direct synthesis of 2-substituted amino ferrocenes where nitrogen is directly attached to the Cp ring was reported by the Metallinos group (Scheme 11).⁴⁴ The BF_3 -complexed dimethylaminoferrocene **38** was found to undergo *ortho*-lithiation upon treatment with *n*-BuLi. When the resulting lithioferrocene was quenched with various carbon and heteroatom based electrophiles, various 1,2-disubstituted products were obtained in 76-94% yield. This included some rare derivatives such as 2-phosphino-1-aminoferrocenes, which were used as ligands for transition metal catalysis.



Scheme 11. BF_3 -mediated synthesis of (±)-2-substituted aminoferrocenes.

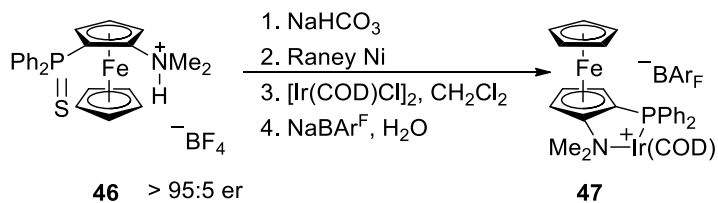
This work was later extended towards the enantioselective synthesis of 2-substituted aminoferrocenes using chiral 1,2-diaminocyclohexane-derived additives. Specifically, we have shown that enantioselective lithiation of BF_3 -activated tertiary aminoferrocenes is possible in the presence of chiral 1,2-diaminocyclohexane ligands to

give a wide range of enantiomerically enriched 2-substituted-1-aminoferrocenes in 90:10 er (80% ee) (Scheme 12).⁴⁵ Both series of enantiomers can be made.



Scheme 12. Asymmetric lithiation of BF_3 -activated aminoferrocenes.

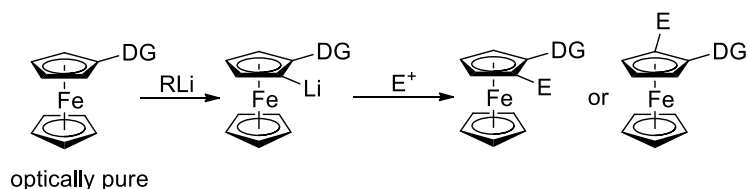
By using this method, the synthesis of rare compounds such as aminophosphine precursor **46** was achieved, and its iridium complex **47** was used for the asymmetric hydrogenation of prochiral alkenes (Scheme 13). Even though this method proves to be feasible for the synthesis of 2-substituted aminoferrocenes, the lower enantioselectivity (up to 80% ee) and lack of manipulability make this method less desirable.



Scheme 13. Synthesis of Ir(I) complex from aminophosphine **46**.

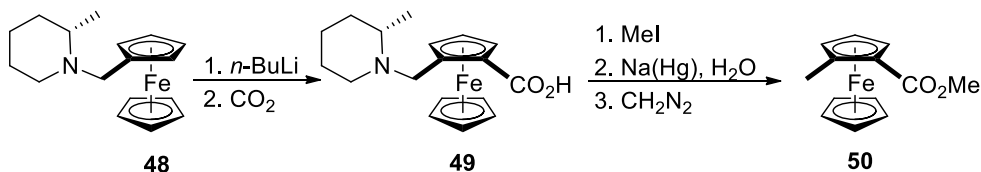
1.1.3.2. Diastereoselective Synthesis of Planar Chiral Ferrocenes

Among the three methods used for the synthesis of planar chiral ferrocenes, diastereoselective-lithiation and substitution is the most widely developed and commonly used. In this method, the chiral auxiliary (usually with *N*- or *O*- lone pair coordinating sites) already present in the molecule coordinates to alkyllithium or lithium dialkylamide bases⁴⁶ thereby differentiating the two possible prochiral *ortho*-positions during deprotonation. Thus the lithioferrocene generated is diastereomerically enriched and may be trapped with electrophiles to afford planar chiral 1,2-disubstituted ferrocenes.²⁹



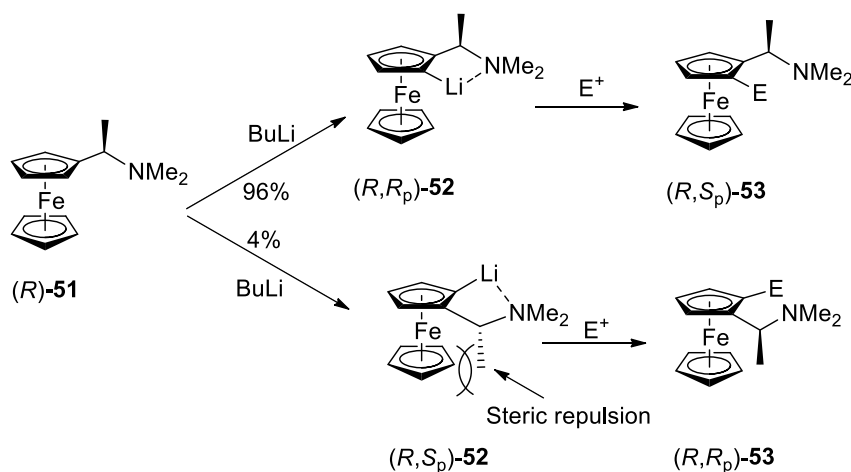
Scheme 14. Diastereoselective lithiation-substitution.

The very first diastereoselective lithiation-substitution reaction was reported by Nozaki and co-workers, making use of a chiral piperidine. After electrophile quench, **49** was converted to (*R_p*)-methyl-2-methylferrocene carboxylate by quaternization with methyl iodide, and subsequent reduction with sodium amalgam in water and esterification with diazomethane. The resulting product was claimed to have formed in 24% yield and 94% optical purity (Scheme 15),^{37, 47} but doubts regarding the diastereoselectivity in lithiation of **48** was reported shortly after.⁴⁸



Scheme 15. Diastereoselective lithiation-substitution by Nozaki.

A significant breakthrough in this field of chemistry was the discovery by Ugi that *N,N*-dimethylferrocenylethylamine effects highly diastereoselective *ortho*-directed lithiation.^{30b} Resolution of (\pm)-**51** with (*R*)-(+)-tartaric acid furnished both isomers in 80-90% yield. Deprotonation of (*R*)-**51** with *n*-BuLi in diethyl ether at 27 °C followed by electrophile quench afforded (*R*, *S_p*)-**53** in 94:6 dr. It has been postulated that the high selectivity in the lithiation originates from unfavourable steric interactions between the stereogenic α -methyl group and the lower Cp ring (*R*, *S_p*)-**52**, as shown in Scheme 16.⁴⁹



Scheme 16. Diastereoselective lithiation-substitution of *N,N*-dimethylferrocenylethylamine.

Compounds prepared from Ugi's amine can further undergo a stereospecific S_N1 type reaction of the dimethylamino moiety with retention of configuration. Figure 3 shows the representative chiral ligands derived from Ugi's amine possessing a methyl group at the stereogenic carbon bonded to C1 (Josiphos **54**, BoPhoz **55**, Walphos **56**, Pigiphos **57** and TRAP **58**).¹⁶ For example, Josiphos is prepared from Ugi's amine by S_N1 type reaction of the dimethylamino group with secondary phosphines, while

Walphos is prepared by transmetalation of ferrocenyllithium species with ZnBr_2 followed by Negishi coupling with bromiodobenzene (Figure 3). TRAP ligands are synthesized by copper-catalyzed homocoupling of 2-iodo ferrocenylphosphine oxide derived from Ugi's amine.

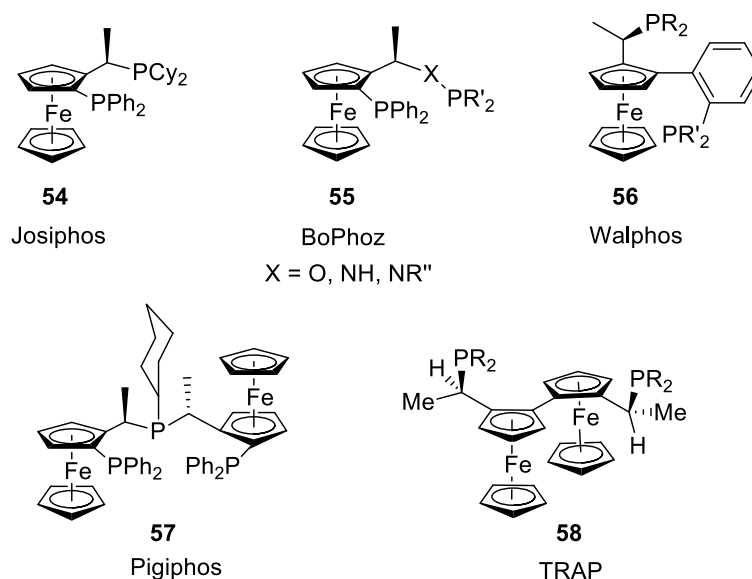
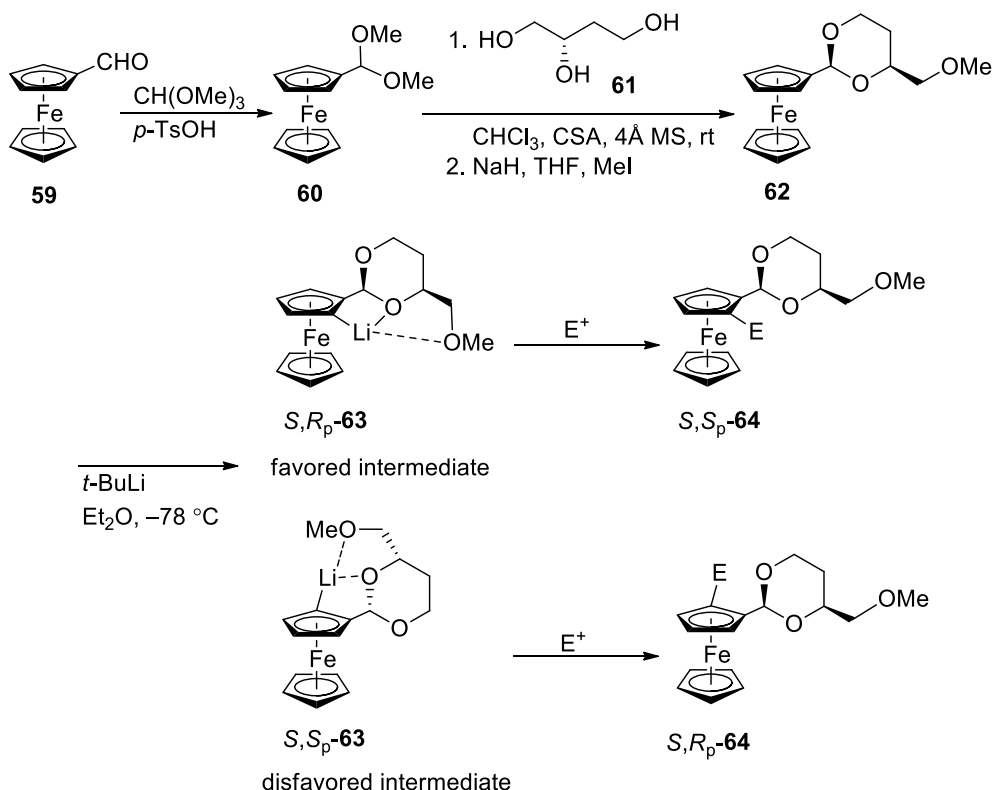


Figure 3. Ferrocenyl ligands derived from Ugi's amine.

Kagan and coworkers in 1993 used a chiral dioxolane moiety for the synthesis of planar chiral ferrocene derivatives.⁵⁰ Ferrocene carboxaldehyde **59** was converted to dimethylacetal **60** using trimethylorthoformate. Transacetalization with (*S*)-1,2,4-butanetriol **61** gave the required acetal as the major product along with other isomeric acetals. Recrystallization from toluene and subsequent methylation afforded (*S,S*_p)-**64** in 85% yield. Selective deprotonation of the prochiral *R* hydrogen of the Cp ring by using *t*-BuLi and electrophile quench proceeded with >98% de. Hydrolysis of the acetal in the presence of *p*-TsOH gave solely planar chiral aldehydes (Scheme 17). In this process, the temperature of the reaction was found to be crucial since the observed diastereoselectivity

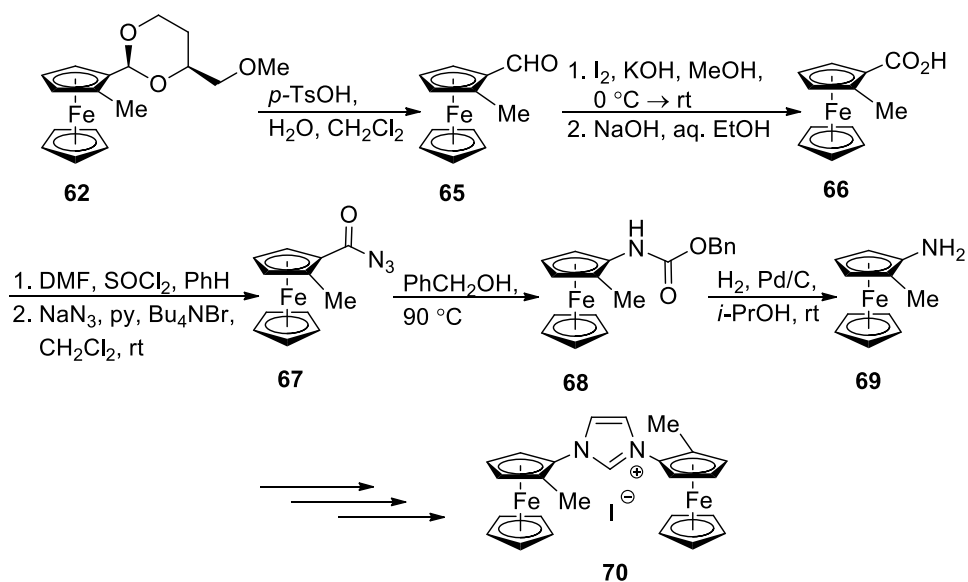
dropped to 80% de at 0 °C. The diastereoselectivity of *ortho*-lithiation was not affected by the presence of substituents, as shown by the use of pentamethylferrocene derivative as substrate.⁵¹



Scheme 17. Diastereoselective lithiation-functionalization using Kagan's acetal.

The chiral acetal **62** was utilized for the synthesis of C_2 -symmetric ferrocenyl ligands.⁵² Togni and coworkers utilized Kagan's acetal to prepare carboxaldehyde **65** which after oxidation was treated with sodium azide to get acyl azide **67**. A Curtius rearrangement furnished the Cbz-protected nitrogen upon deprotection afforded the 2-methyl-1-aminoferrocene **69** which was used to make the chiral *N*-heterocyclic carbene ligand (Scheme 18).^{52b} It took seven steps including the use of an acyl azide which can potentially be explosive to incorporate nitrogen directly to the Cp ring. Togni stated that

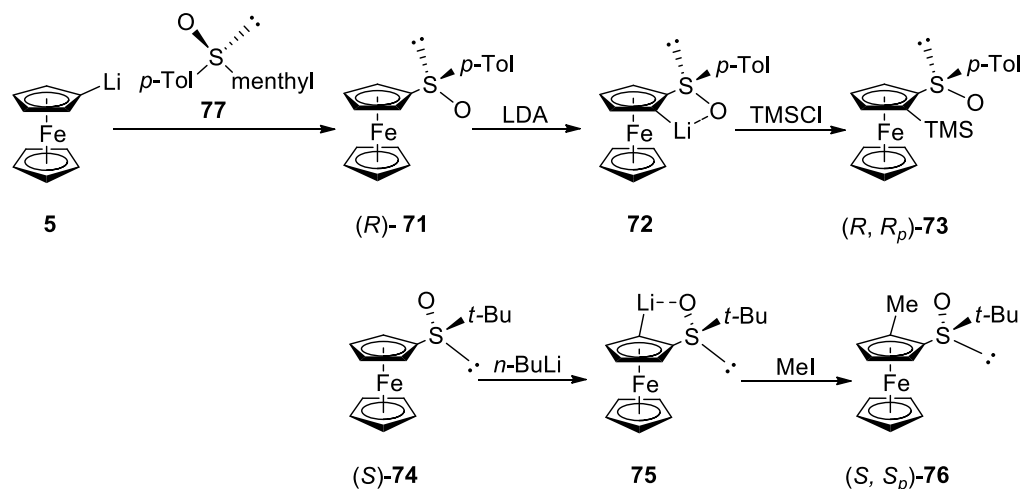
the major challenge of their synthesis was the introduction of a nitrogen bond directly onto the Cp ring. Later on, the same group reported the preparation of aminoferrocenes in five steps starting from Ugi's amine.^{52a} Even though the number of steps was shortened to five, the synthesis still required the preparation of DPPA (diphenyl phosphoryl azide) and relies on a diastereoselective nucleophilic addition to the alkene, whose stereoselectivity varies with the nucleophile.



Scheme 18. Synthesis of planar chiral ligands using acetal directing group.

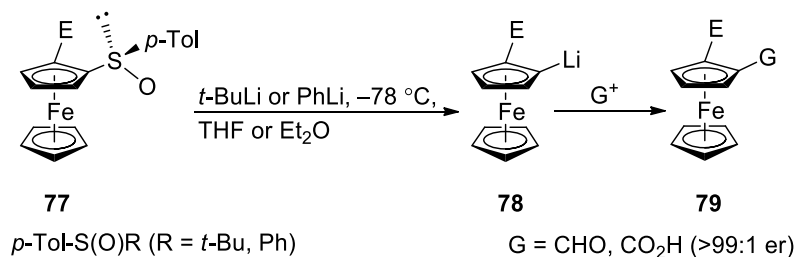
The use of chiral sulfoxides for diastereoselective-lithiation and substitution was reported initially by Kagan and coworkers in 1993 (Scheme 19).⁵³ The key sulfoxide (*R*)-**71** was synthesized by transmetalation of tributylstannyl ferrocene to lithioferrocene and electrophile quench using optically pure menthyl *p*-toluenesulfinate. Transmetalation was necessary since the presence of excess lithioferrocene caused racemization of the sulfoxide (*R*)-**71**. To avoid this, new methods were developed which included enantioselective oxidation of ferrocenyl sulphides⁵⁴ or the use of other chiral sulfinates

such as Ellman's reagent.⁵⁵ As shown in Scheme 18, the enantiopure *t*-Bu ferrocenyl sulfoxide can be deprotonated with *n*-BuLi and quenched with iodomethane to afford the 1,2-disubstituted product (*S*, *S_p*)-**76** in 98:2 dr. While its *p*-tolyl congener, upon diastereoselective lithiation-electrophile quench, gave (*R*, *R_p*)-**73** in 99:1 dr.⁵⁶



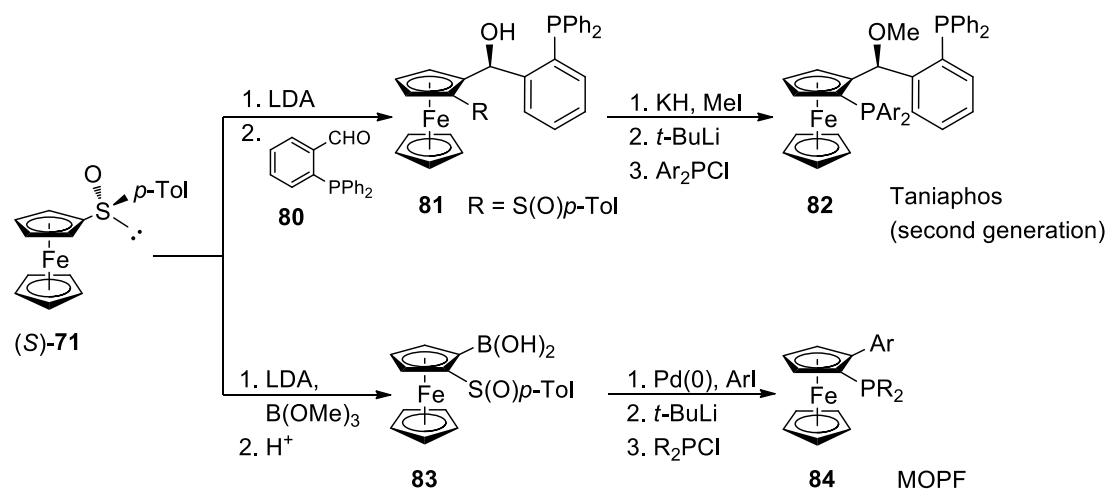
Scheme 19. Diastereoselective *ortho*-lithiation of ferrocenyl sulfoxides.

The sulfoxide moiety can be easily converted to other functional groups, giving this method a large degree of flexibility.⁵⁴ Sulphur-lithium exchange with PhLi⁵⁷ or *t*-BuLi⁵⁶ gave intermediate **78** which can be trapped with various electrophiles to give planar chiral 1,2-disubstituted ferrocene compounds (Scheme 20). However, this requires that the substituents introduced must be stable to strong bases or be protected.



Scheme 20. The synthesis of planar chiral 1,2-disubstituted ferrocenes.

This strategy was utilized for the synthesis of diverse ligands.²⁹ The second generation Taniaphos was synthesized by *ortho*-lithiation of (*S*)-**71** with LDA and quench with *ortho*-phosphinyl benzaldehyde to afford alcohol **81** which was methylated (Scheme 21). Sulfoxide-lithium exchange using *t*-BuLi followed by electrophile quench using chlorodiarylphosphine gave **82**.⁵⁸ Similar series of transformations using B(OMe)₃ gave boronic acid **83**, which underwent Suzuki coupling with iodoarenes. Sulfoxide-lithium exchange and chlorodiaryl phosphine quench furnished MOPF **84**.⁵⁹

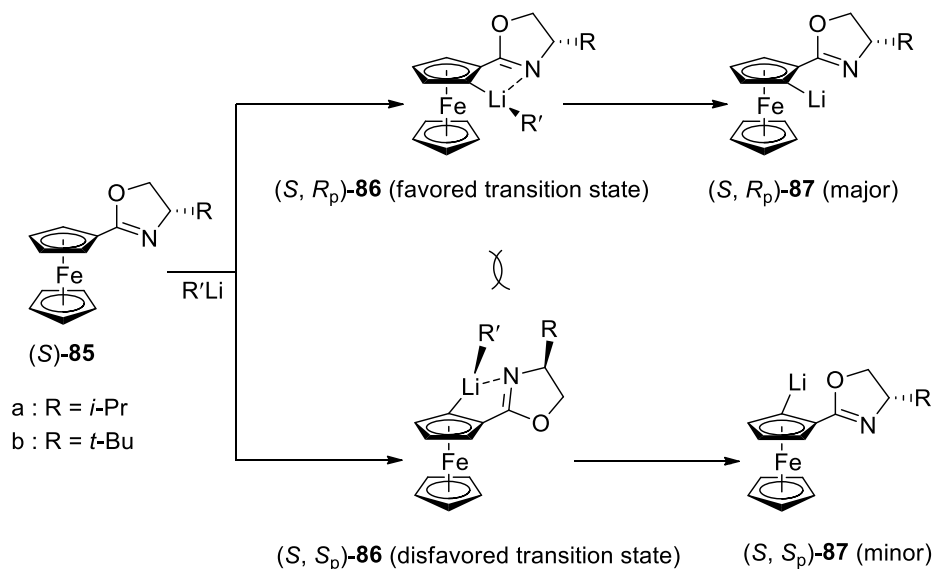


Scheme 21. Synthesis of planar chiral ligands using ferrocenyl sulfoxides.

All the directing groups mentioned so far need to be modified or replaced with *P*, *S*, or *N* substituents to make them suitable donor ligands. In the case of chiral oxazolines, they act as directing groups as well as excellent *N*-donor ligands. Ferrocenyl oxazolines can be synthesized by using commercially available ferrocene carboxylic acid and optically pure amino alcohols. The use of these compounds in diastereoselective-lithiation was reported independently by Richards,⁶⁰ Sammakia⁶¹ and Uemura.⁶² When

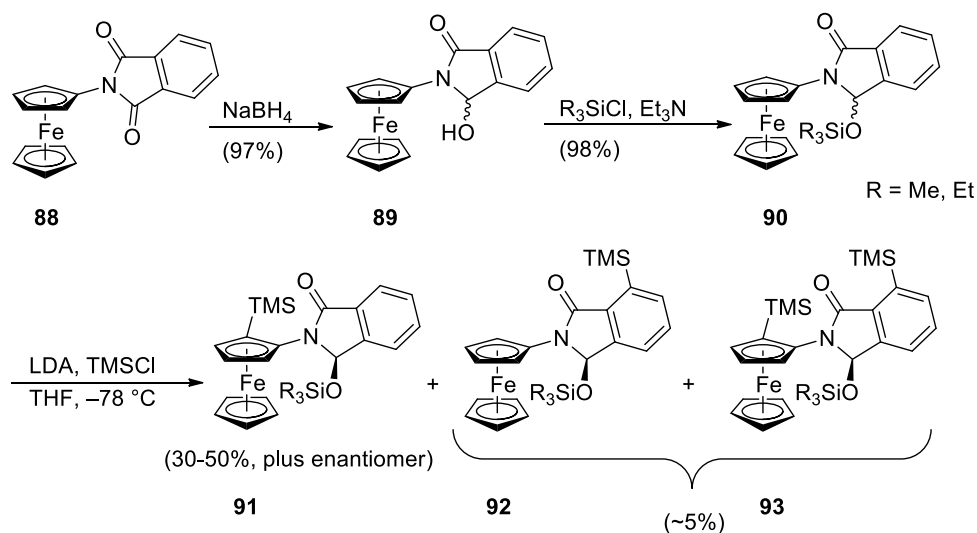
(*S*)-**85** was treated with *n*-BuLi or *s*-BuLi in ether at $-78\text{ }^{\circ}\text{C}$, selective removal of the prochiral *R* hydrogen occurred in up to 39:1 diastereomeric ratio. The diastereoselectivity can be further increased to >500:1 by changing the solvent to hexanes and by adding TMEDA.^{61a} The high diastereoselectivity in the case of these compounds can be attributed to the avoidance of steric interaction between the alkyl group of the alkyllithium reagent with the substituent on the oxazoline center (Scheme 22). Upon addition of TMEDA, the effective size of alkyllithium reagent increases by chelating to it, thereby increasing the steric repulsion between *R* and *R'*, hence causing a dramatic increase in diastereoselectivity.²⁹

Numerous multidentate ferrocenyl ligands containing chiral oxazolines have been reported, and have found applications in Pd- catalyzed allylic alkylation and amination,⁶³ and intermolecular asymmetric Heck reactions.⁶⁴



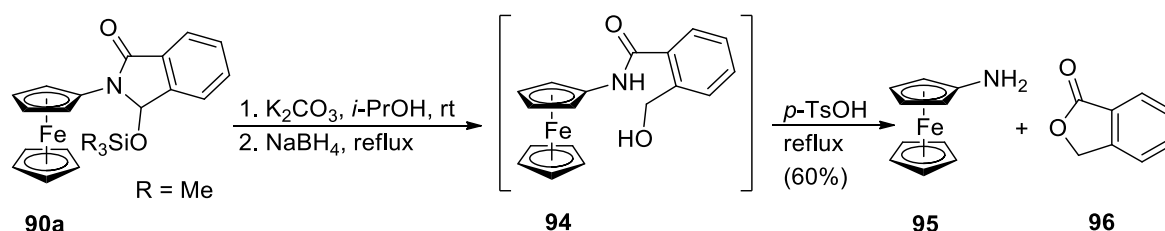
Scheme 22. Diastereoselective lithiation-substitution of ferrocenyl oxazoline.

Previous work in our group used diastereoselective synthesis of planar chiral ferrocenes using ferrocenyl phthalimidine as a directing group (Scheme 23).⁶⁵ The phthalimidine group was designated to leave nitrogen on the product and its inherent lability allowed further transformations. Hence this approach avoided the needs to introduce nitrogen at a later stage of synthesis and protection-deprotection sequences and rearrangement reactions. *N*-Ferrocenylphthalimide was prepared from ferrocene following the procedures of Bildstein¹⁴ and Sato.⁶⁶ Thus, iodoferrocene was coupled with phthalimide by Cu₂O mediated coupling in pyridine. When ferrocenyl phthalimide was reduced and protected; ferrocenyl phthalimidine **90** containing a β-ferrocenyl stereocenter was obtained. When **90** was subjected to lithiation conditions using LDA and quenched with ClSiMe₃, gave the 2-silylated product **91** as the major product along with inseparable mixture of two aryl-silylated products in less than 5% combined yield (Scheme 23). An important observation from this reaction was that **91** was a diastereomerically pure compound by ¹H and ¹³C NMR. This shows that the lithiation occurred in ≥95:5 diastereoselectivity.



Scheme 23. Diastereoselective substitution of phthalimidines.

In addition, the phthalimidine moiety can easily be deprotected and reduced by sequential addition of K_2CO_3 and $NaBH_4$ to give the hydroxyamide **94** which could be cleaved to give aminoferrocene and phthalide (Scheme 24).⁶⁷ Hence it can be stated that if the phthalimidine starting material was a single stereoisomer, then Cp-silylation followed by deprotection of nitrogen to primary amine⁶⁸ would afford product with solely planar chirality.

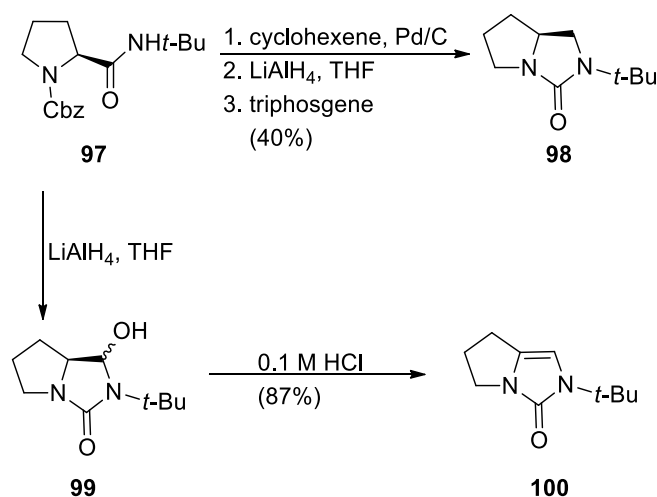


Scheme 24. One-pot deprotection of *O*-SiR₃ phthalimidines.

1.1.3.3. Nitrogen-Based Chiral Auxiliaries in Lithiation-Substitution Reactions

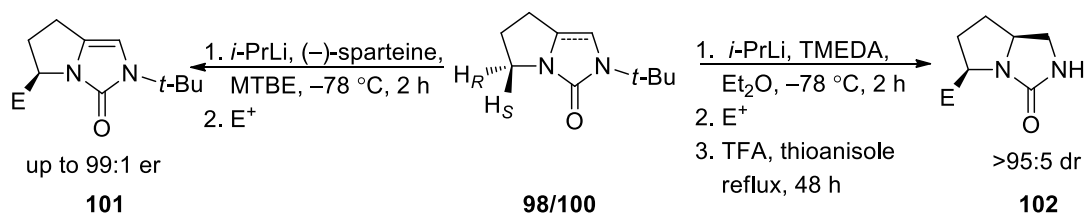
The use of nitrogen-based directing groups is common in arene lithiation and metal catalyzed C-H activation reactions, but not well exploited in ferrocene substitution reactions. A good chiral auxiliary is one that can be easily attached to a substrate in one enantiomeric form to give products in high diastereomeric ratio and can be easily cleaved from the product.

Metallinos and coworkers have reported a directing group that would facilitate diastereo- as well as enantioselective lithiation reactions using readily available and inexpensive L-proline as a starting material (Scheme 25).⁶⁹ The required starting materials were prepared from *t*-Bu amide **97**, which was obtained from Cbz-protected L-proline.



Scheme 25. Preparation of starting materials.

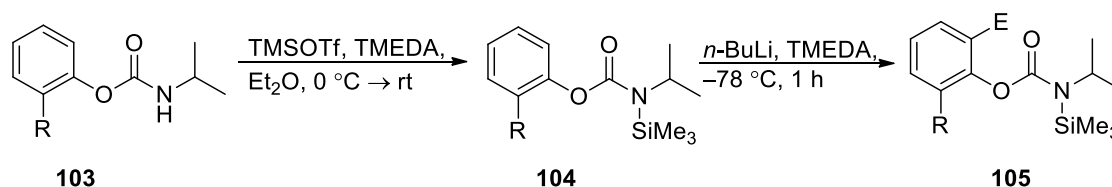
The chiral urea **98** underwent selective deprotonation of the pro-*S* hydrogen using *s*-BuLi, followed by electrophile quench to afford products in >95:5 diastereoselectivity. When the achiral imidazolones were used, asymmetric lithiation using *i*-PrLi in presence of (–)-sparteine occurred which up on electrophile quench afforded products in up to 99:1 er. The resulting products were successfully converted to ligand precursors and organocatalysts.



Scheme 26. Diastereo/enantioselective lithiation-substitution of urea.

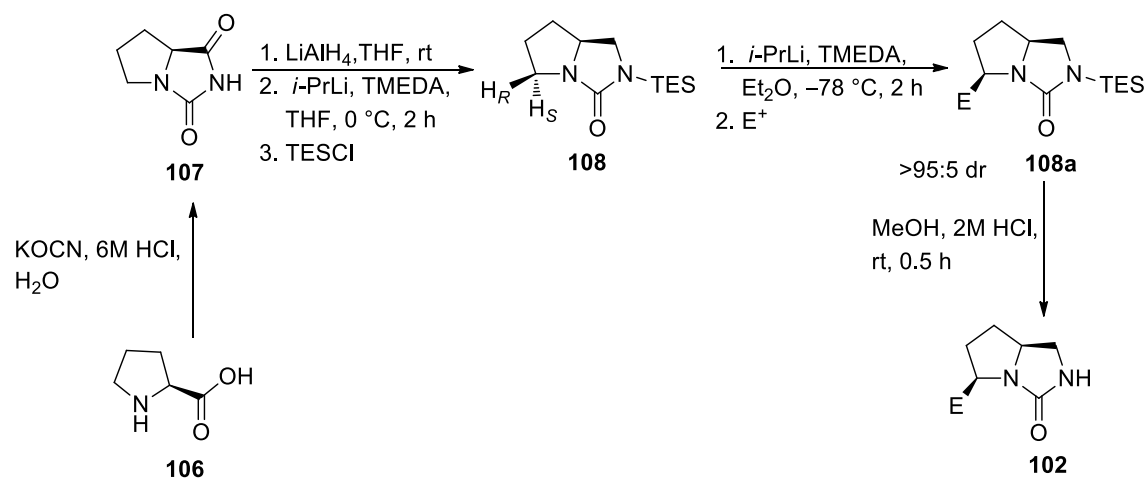
The difficulty in removing the *t*-Bu group initiated a further improvement of this strategy. Hoppe and coworkers have shown that when *N*-silyl protected *O*-aryl carbamates were subjected to *ortho*-lithiation, a broad range of *ortho*-substituted products

105 were obtained.⁷⁰ The removal of the carbamate moiety under basic conditions furnished *ortho*-substituted phenols.



Scheme 27. *ortho*-lithiation by *N*-silyl *O*-aryl carbamates.

Hence we decided to use *N*-silyl protected L-proline hydantoin moiety as a directing group to achieve diastereoselective lithiation-substitution of **108** (Scheme 28).⁷¹ Similar selectivity was observed for **108**, as was seen in the case of **98**. Deprotection of the silyl group under acidic conditions furnished **102**, which was utilized for the synthesis of organocatalysts (chiral guanidines) and metal complexes. Thus the L-proline hydantoin derived chiral auxiliary proved to be less expensive and required fewer synthetic steps compared to *N*-Cbz protected prolinamide **97**.



Scheme 28. Diastereoselective lithiation-substitution using *N*-silyl protected **108**.

1.2. Asymmetric Hydrogenation of 2-Substituted Quinolines

1.2.1. Applications of Tetrahydroquinolines

The tetrahydroquinoline ring systems form a common structural motif found in a number of pharmaceutical agents and are found as the core structure of a number of natural products.⁷² For example, (*S*)-flumequine **109** is an antibacterial agent.⁷³ Some of the simple 2-substituted 1,2,3,4-tetrahydroquinoline alkaloids isolated from the trunk bark of a Venezuelan shrubby tree *Galipea officinalis* Hancock, is known in folk medicine for its many healing properties (Figure 4).⁷⁴ Apart from the broad applications in pharmaceutical and agrochemical synthesis, these compounds have been used as coordination ligands as well.⁷⁵

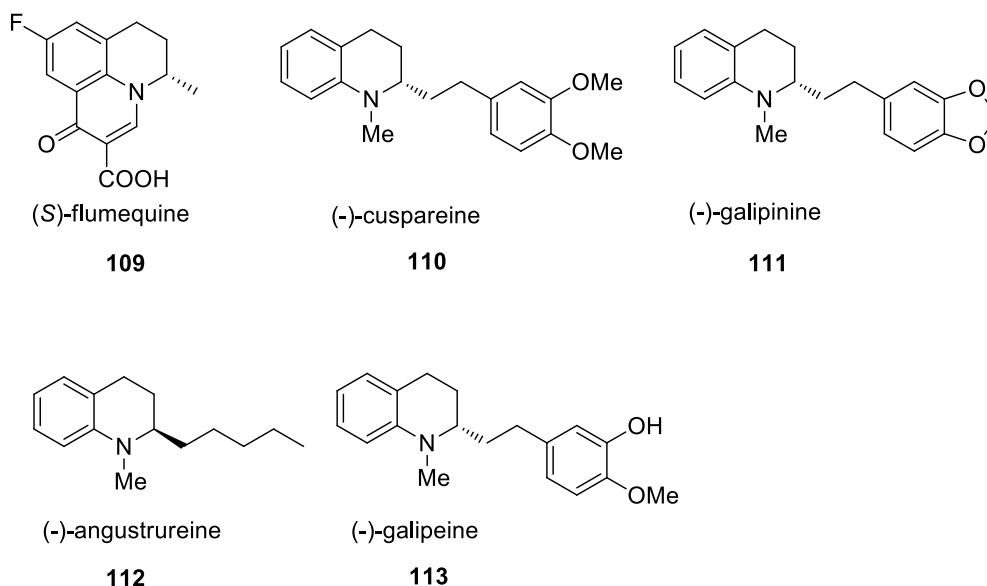
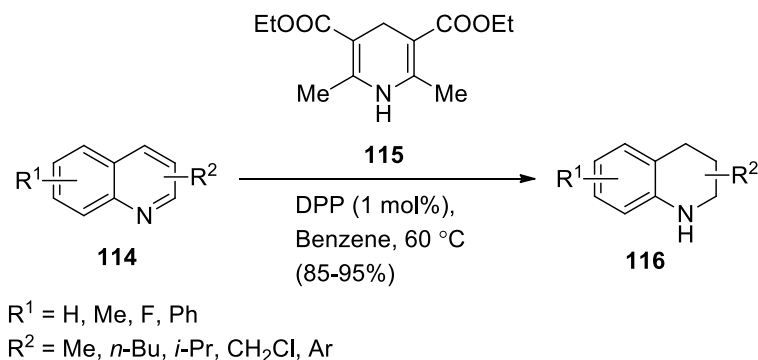


Figure 4. Selected bioactive compounds and alkaloids derived from chiral 1,2,3,4-tetrahydroquinoline derivatives.

1.2.2. Hydrogenation of Quinolines

The partial hydrogenation of polynuclear heteroaromatics using H₂ was first reported by Fish and coworkers in 1982 using a ruthenium catalyst.⁷⁶ Later on, various

methods such as the use of transition metals, metals in acids (Sn/HCl, Zn/HCOOH, Zn/CH₃COOH), cobalt or Raney nickel catalyzed hydrogenations, as well as acid catalyzed transfer hydrogenation in presence of Hantzsch ester were developed for the reduction of quinoline derivatives (Scheme 29).^{72a, 77}



Scheme 29. Organocatalytic hydrogenation of quinolines.

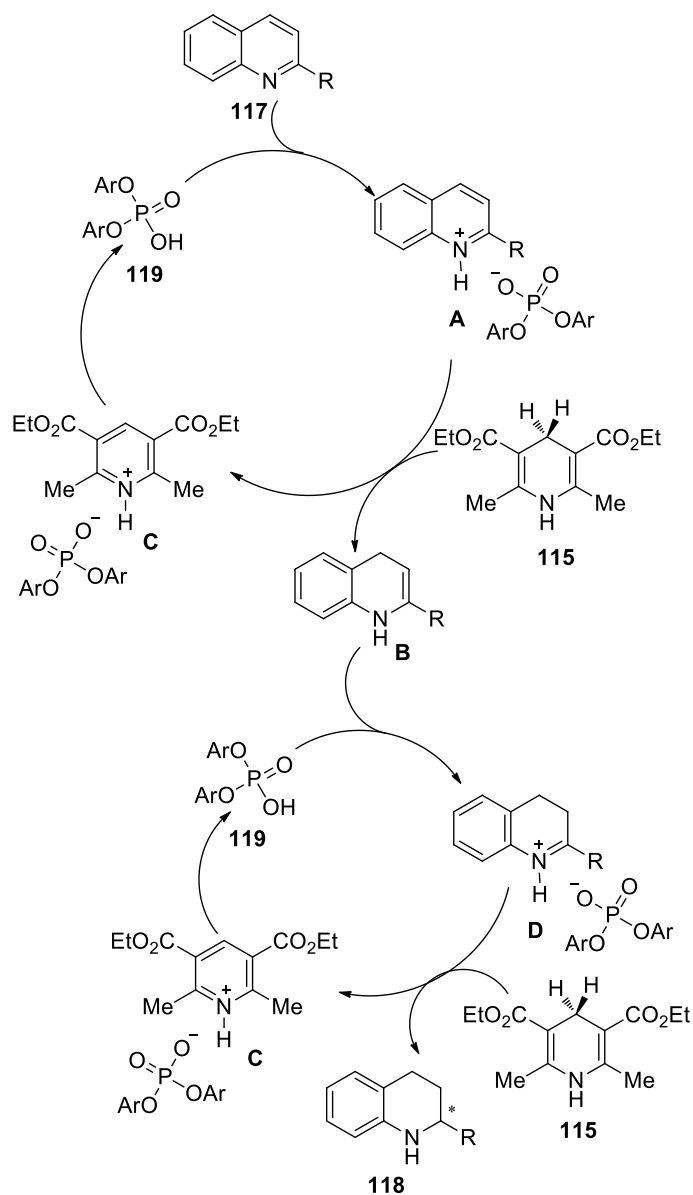
1.2.3. Asymmetric Hydrogenation of Quinolines

The asymmetric hydrogenation of heteroarenes is rather difficult compared to other prochiral unsaturated compounds, such as olefins, ketones, and imines. The high stability of aromatic compounds, the presence of a heteroatom that can potentially deactivate the catalyst, and the lack of secondary coordinating groups make it difficult to get high activity and/or enantioselectivity.⁷⁸ Among them, bicyclic heteroaromatic compounds are easy to hydrogenate compared to the corresponding single ring systems as one of the rings is reserved for hydrogenation process.

1.2.3.1. Brønsted Acid-Catalyzed Asymmetric Hydrogenation

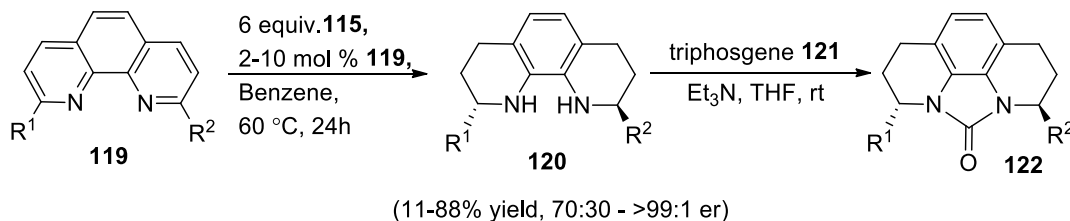
The use of chiral phosphoric acids in the chiral Brønsted acid-catalyzed asymmetric transfer hydrogenation⁷⁹ of quinolines was first reported by Rueping.⁸⁰ The

The key step in this mechanism varies with the position of substituents. For 2-substituted quinolines, the stereodetermining step was the Brønsted acid-catalyzed 1,2-hydride addition. However, in the case of 3-substituted quinolines, isomerization of **B** promoted by Brønsted acid to give **D** was the key step. Rueping used this methodology for the asymmetric transfer hydrogenation of 3- and 2,3-substituted quinolines *via* an enantioselective protonation process as well.^{80b}



Scheme 31. Proposed mechanism for asymmetric hydrogenation of quinolines.

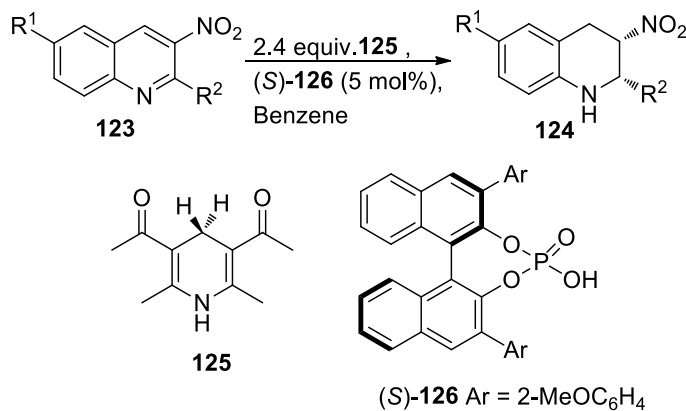
Rueping's method was also applied to 2- and 2,9- octahydrophenanthrolines by the Metallinos group and it was observed that the transformations of phenanthrolines were difficult compared to analogous quinolines.⁸¹ The enantioselectivity and conversion were found to be dependent on the steric bulk of the substituents in R¹ position. For smaller substituents, reduction products were obtained in ~ 50% yield with 90:10 er as diamine products (Scheme 32). Conversion to corresponding ureas **122** allowed the measurement of enantioselectivity using chiral HPLC. The introduction of bulkier groups led to an erosion in the yields and enantioselectivities (R¹ = *i*-Pr, 28% yield, 70:30 er). Surprisingly, 2-phenyl phenanthroline was reduced in low yield, but with excellent er (97:3), while 2,9-diphenylphenanthroline underwent reduction of only one pyridyl ring in high yield and lower er (62:38). A secondary interaction such as π -stacking was suggested for this anomalous behaviour.



Scheme 32. Organocatalytic reduction of 2- and 2,9- disubstituted phenanthrolines.

Very recently, Zhou and coworkers reported asymmetric transfer hydrogenation of 3-nitroquinolines with high enantio- and distereoselectivities (Scheme 33).⁸² The original experiment using [Ir]/(*S*)-MeO-Biphep **139**/I₂ [(*S*)-MeO-Biphep = (*S*)-(2,2'-dimethoxybiphenyl-6,6'-diyl)bis(diphenyl phosphine)] afforded the desired product only in 16% yield and 19% ee, presumably due to the increased aromaticity arising from the

presence of the nitro group and its interaction with the catalyst. Using chiral acid (*S*)-**126** and Hantzsch ester **125**, enantiomerically enriched cyclic nitro compounds with two continuous stereocenters were synthesized (Scheme 33).



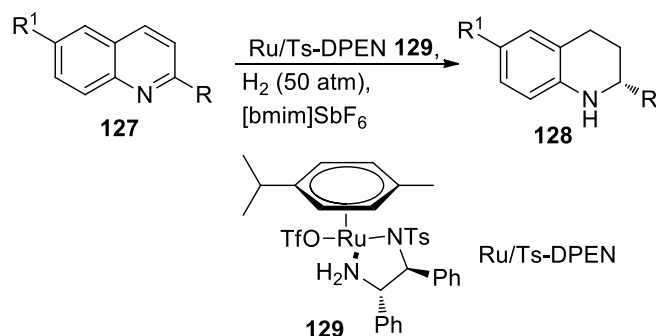
Scheme 33. Organocatalytic reduction of 3-nitroquinolines.

1.2.3.2. Ruthenium and Rhodium-Catalyzed Asymmetric Hydrogenation

Even though iridium is the most widely used metal, other transition metals such as ruthenium and rhodium are also used in the asymmetric hydrogenation of quinolines in the presence of chiral ligands. An air stable Ru/Ts-DPEN catalyst in ionic liquid was found to be excellent for asymmetric hydrogenation of quinolines with quantitative conversions and enantioselectivities up to 99%.⁸³ This catalyst system introduced by Chan and Fan was found to proceed smoothly in MeOH and ionic liquid [bmim]PF₆ (Scheme 34) and was found to be selective towards C=N (quinoline) over C=O (ketone) bonds. By using a thin film of ionic liquid supported on silica gel, the reusability of catalyst up to sixth run by simple filtration was achieved.

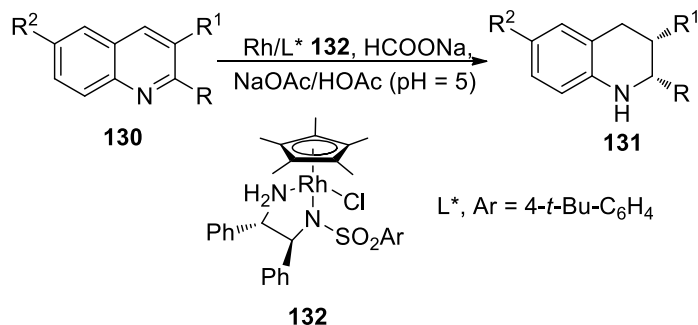
Other notable works in this area included the use of solvent-free or highly concentrated systems which gave high conversion and selectivity,⁸⁴ and the use of

tethered Ru(II) complex in a solution of formic acid/triethylamine/methanol which gave moderate enantioselectivities with good conversion in contrast to Ru/TsDPEN system.⁸⁵



Scheme 34. Ruthenium catalyzed asymmetric hydrogenation of quinolines.

An asymmetric transfer hydrogenation of quinolines were carried out by Xiao and coworkers, using a $[\text{Cp}^*\text{RhCl/Ts-dpen}]$ catalyst system (Ts-dpen = *N*-(*p*-toluenesulfonyl)-1,2-diphenylethylenediamine, Noyori ligand)⁸⁶ in aqueous media.⁸⁷

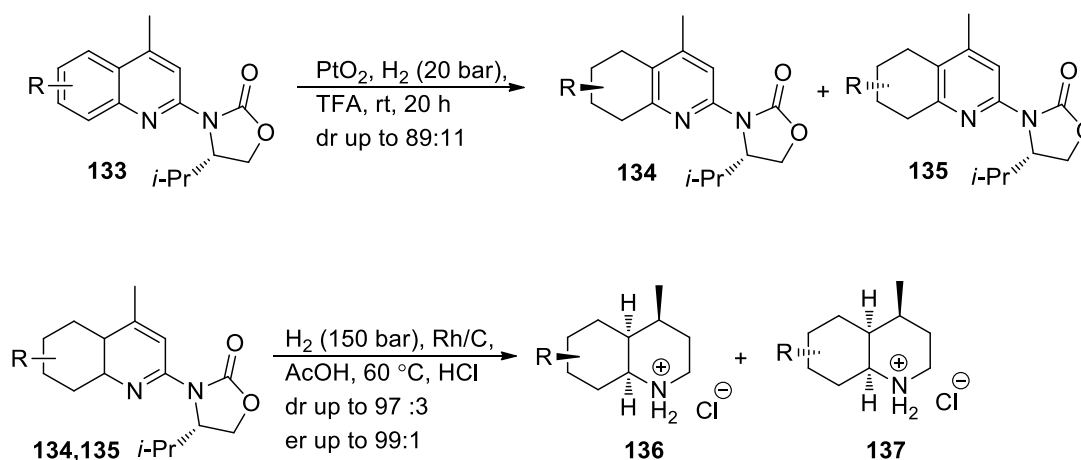


Scheme 35. Rh-catalyzed asymmetric transfer hydrogenation of quinolines.

The reaction rate was found to be sensitive to the pH of the reaction medium and on the concentration of both formate and protonated quinolines. This supported the proposed ionic mechanism. The best reactivity and selectivity were observed with 4-*tert*-butylphenyl-substituted ligand (Scheme 35). A broad range of substrates, 2-alkyl, 2-aryl,

2,3-disubstituted and 2,6-disubstituted quinolines gave desired products in good conversions and high enantioselectivities.

A diastereoselective hydrogenation using a chiral auxiliary-substituted quinolines was carried out by Glorius and coworkers (Scheme 36).⁸⁸ The usual homogenous asymmetric hydrogenation involves formation of 1,2,3,4 tetrahydroquinolines with a newly formed stereocenter at 2- and/or 3- positions. This reaction stands out from others as it gave 5,6,7,8 tetrahydroquinolines. The reaction was carried out with two consecutive heterogeneous hydrogenations. In the first step, PtO₂ and trifluoroacetic acid were found to be the optimal combination to give 5,6,7,8 tetrahydroquinolines in good yield and dr up to 89:11. These were then taken to the next step, where catalytic hydrogenation and Rh/C with acetic acid as solvent gave decahydroquinolines with four newly formed stereocenters with enantioselectivities up to 99% ee, which also enabled complete removal of the auxiliary. The *cis*-stereochemistry was controlled by the chiral auxiliary rather than the methyl group present.



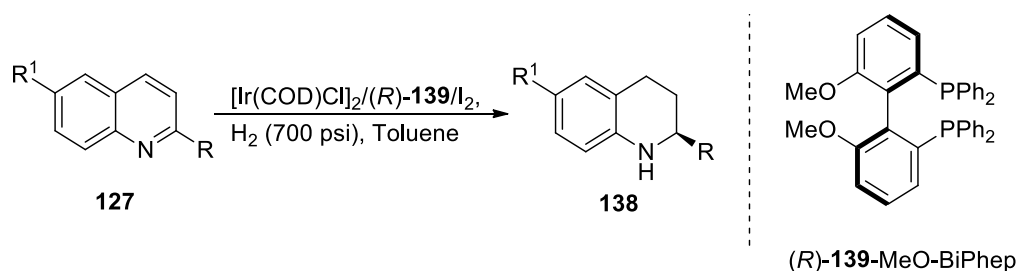
Scheme 36. Diastereoselective hydrogenation of quinolines to decahydroquinolines.

1.2.3.3. Iridium-Catalyzed Asymmetric Hydrogenation

Iridium catalyzed asymmetric hydrogenation⁸⁹ of quinolines has proven to be the mostly widely used method to access enantiopure 1,2,3,4 tetrahydroquinolines. A vast number of studies have been done in this area mostly focusing on finding effective ligands to get high activity and selectivity. A variety of bidentate phosphorus ligands such as atropisomeric biaryl diphosphine ligands, diphosponite ligands and phosphine-phosphoramidite ligands and some monodentate as well as phosphorus containing ligands such as *N,P*-ligands and *S,P*-ligands, have been used. Additives such as iodine, chloroformates, Brønsted acids and triphenyl phosphine were needed in some cases.^{72a}

1.2.3.4. Atropisomeric Biaryl Diphosphine Ligands

A significant lead in this field was a highly effective Ir-catalyzed asymmetric hydrogenation of 2,6-substituted quinolines reported by Zhou and co-workers in 2003 using (*R*)-MeO-Biphep **139** as the ligand in the presence of iodide.⁹⁰



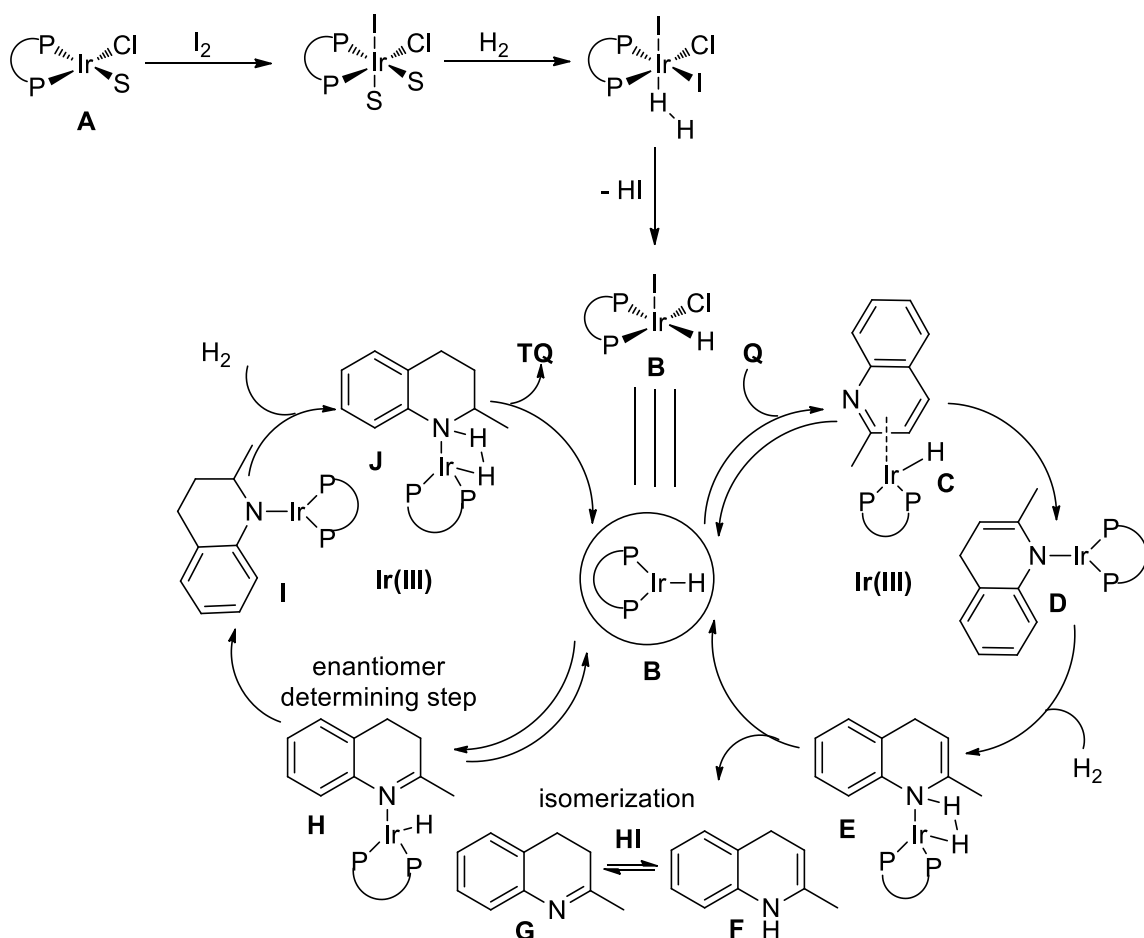
Scheme 37. Ir-catalyzed asymmetric hydrogenation of quinolines.

Their initial studies on the hydrogenation of 2- methyl quinoline as a model substrate and $[\text{Ir}(\text{COD})\text{Cl}]_2/(\text{R})\text{-MeO-Biphep}$ **139** as the catalyst system in CH_2Cl_2 provided product with low enantioselectivity. Screening of different additives showed that the addition of iodine increased both activity and selectivity. The reaction was found

to be strongly solvent dependant, and toluene provided the best reaction media. Under the optimal conditions, different 2- and 2,6-substituted quinolines were hydrogenated with high conversions (83-94% yield) and enantioselectivities (72-96% ee). Using this catalyst system, alkyl, aryl, benzylic and 2,3- substituted quinolines were hydrogenated.⁹¹ This catalyst had good functional group tolerance as well. Various functional groups such as hydroxyl, ketone, ester, amide benzenesulfonyl substituted quinolines were hydrogenated using benzene as solvent media.

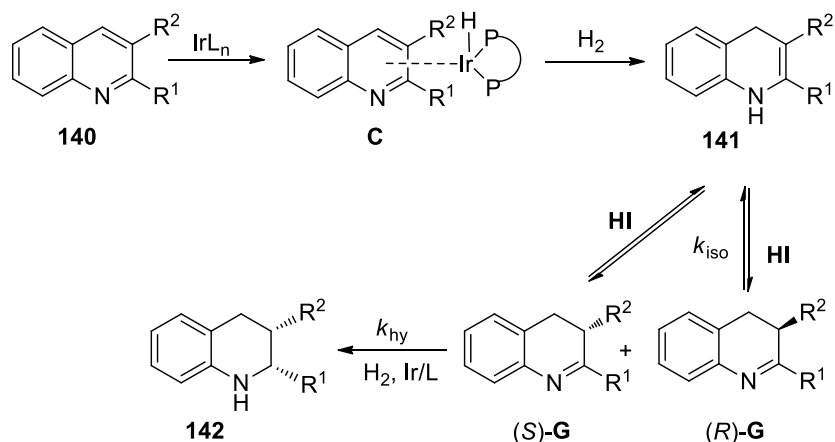
The methodology was extended towards the synthesis of natural products cuspareine **110**, galipinine **111**, augustureine **112** and the first enantioselective total synthesis of naturally occurring alkaloid (–)-galipeine **113**.^{74b}

The studies on the mechanism and on the role of iodine were conducted by experimental and computational studies by Zhou *et al.* (Scheme 38).⁹¹ The reaction proceeded *via* two catalytic cycles and an inner sphere mechanism was postulated. In the presence of I₂, the Ir(I) species **A**, is oxidized to generate an Ir(III) species and subsequent heterolytic cleavage of H₂ gives the Ir(III)-H species **B** with the release of HI. The coordination of quinoline to **B** generates **C** and a 1,4-hydride transfer provides intermediate **D**. Heterolytic cleavage of another molecule of H₂ gives enamine **F** and regenerates the Ir(III)-H catalytic species **B**. Isomerization of **F** in presence of HI forms imine **G**, which then enters a second catalytic cycle where it is coordinated to the active catalytic species **B** to give intermediate **H**. This is the stereo-determining step where insertion of Ir-H to the C=N generates the chiral center which further undergoes a σ -bond metathesis with hydrogen to generate tetrahydroquinoline and regenerates the catalyst, thus completing the cycle.



Scheme 38. Postulated mechanism for Ir-catalyzed hydrogenation of quinolines.

In the case of 2,3-disubstituted quinolines, the stereodetermining step is the isomerization of **F** to **G**, followed by hydrogenation to provide product by a kinetic resolution process. For high enantioselectivity, the rate of isomerization (k_{iso}) should be faster than rate of hydrogenation (k_{hy}) (Scheme 39). Hence to accelerate isomerization and decelerate the hydrogenation high temperature and low hydrogen pressure should be employed.⁹¹



Scheme 39. Mechanism for hydrogenation of 2,3-disubstituted quinolines.

In 2005, Chan and coworkers reported the use of P-Phos **143a** for asymmetric hydrogenation of quinolines and up to 92% ee was obtained. The catalyst was found to be air stable and subsequently its recyclability was tested in DMPEG-500/hexane. The catalyst retained its activity and enantioselectivity up to eight cycles and only a simple filtration was necessary to isolate the products. Further studies showed that the efficiency of this catalyst can further be increased if used with degassed solvent in a glovebox. Its catalyst activity increased with a decrease in the amount of iodine, which reduced catalyst loadings to S/C ratio 2000-50000 as well. Under these conditions, products were obtained in excellent yields and up to 96% ee with up to 4000 h^{-1} TOF and 43000 TON.^{78, 92}

Following this report a series of C_2 -symmetric diphosphine ligands were synthesized by Chan and coworkers using atropdiastereoselective Ullmann coupling and ring-closure reactions, which were subsequently tested for asymmetric hydrogenation of quinolines, looking for air stable and recyclable ligands (Figure 5).⁹³ The reactions proceeded well in DMPEG-500/hexane while poor conversion and enantioselectivity were obtained when carried out in ionic liquids. Iridium catalysts of P-Phos **143a**, Xyl-P-

Phos **143b** and Cl-MeO-Biphep **144** were found to be air stable, however catalysts derived from SynPhos **145** and Difluorophos **146** ligands were sensitive to air. By using 2-methyl quinoline as substrate, the catalyst reproducibility was tested in DMPEG/hexane system and found that Ir-MeO-Biphep **139**, Ir-Cl-MeO-Biphep **144** and Ir-SynPhos **145** were suitable for catalyst recovery and reuse.^{93a} The commercially available DifluorPhos **146** with $[\text{Ir}(\text{COD})\text{Cl}]_2$ in THF forms a very efficient catalyst with TON up to 43000 and TOF up to 3510 h^{-1} .⁷⁸

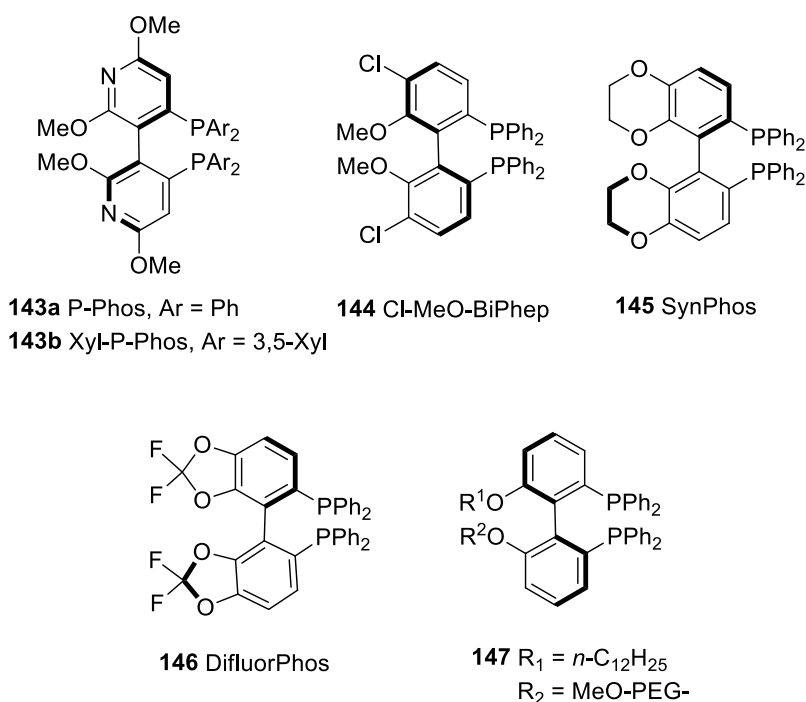


Figure 5. Atropisomeric diphosphine ligands for asymmetric hydrogenation.

A major drawback for most of these catalytic systems for quinoline hydrogenation was low catalyst activity; to achieve good results, a low substrate/catalyst ratio of 100 was needed. This is because of catalyst deactivation that arises from the formation of dimers and trimers through hydride bridged bonds under hydrogen atmosphere.⁹⁴ To

prevent this, modifications were done to ligands, either by using dendrimers to encapsulate the iridium complex or through the introduction of bulky substituents **147**.⁹⁵

1.2.3.5. Diphosphinite and Diphosphonite Ligands

The use of chiral diphosphinite ligands in asymmetric hydrogenation of quinolines were investigated by Chan's group (Figure 6).⁹⁶ Comparing BINAPO **148a** and H8-BINAPO **148b**, the latter gave better results resulting from its rigid structure with up to 96% ee was obtained when reaction was carried out in THF and even better results in DMPEG-500/hexane.

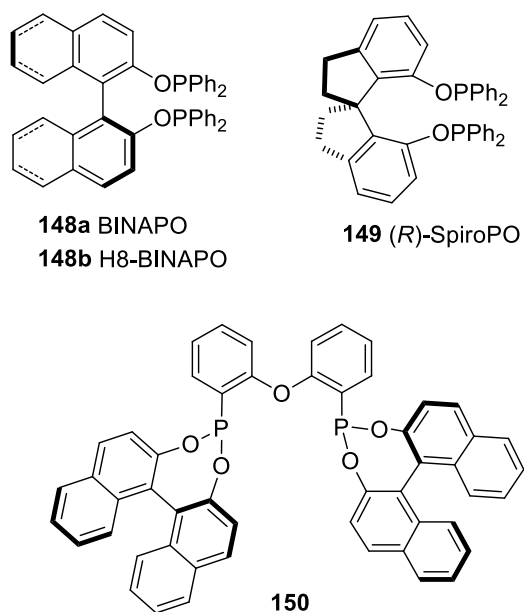


Figure 6. Diphosphinite and diphosphonite ligands.

The iridium catalyst was prone to deactivation in this system, its activity and enantioselectivity dropped after two runs. The rigidity of the spirobiindane system to facilitate chirality transfer and prevent catalytically inactive species was utilized by Chan and coworkers (Figure 6); their SpiroPO ligand **149** showed superior activity and

selectivity with S/C ratio of 5000. However, the recyclability of this catalyst system in DMPEG-500/hexane biphasic system showed a sharp drop in conversion.⁹⁷ A BINOL-derived diphosphinite ligand **150** with an achiral diphenyl ether link was used by Reetz and coworkers. To further improve the enantioselectivity, achiral monodentate P-ligands were used as additive for some substrates.⁹⁸

1.2.3.6. Other Phosphine-Containing Ligands

Franciò and Leitner *et al.* developed a set of phosphine-phosphoramidite ligands **151**, which possesses two elements of chirality and were found to be effective in Rh-, Ru- and Ir- catalyzed asymmetric hydrogenation reactions (Figure 7). Hence these fall into the category of privileged ligands. In the Ir-catalyzed hydrogenation of quinolines, up to 97% ee was obtained.

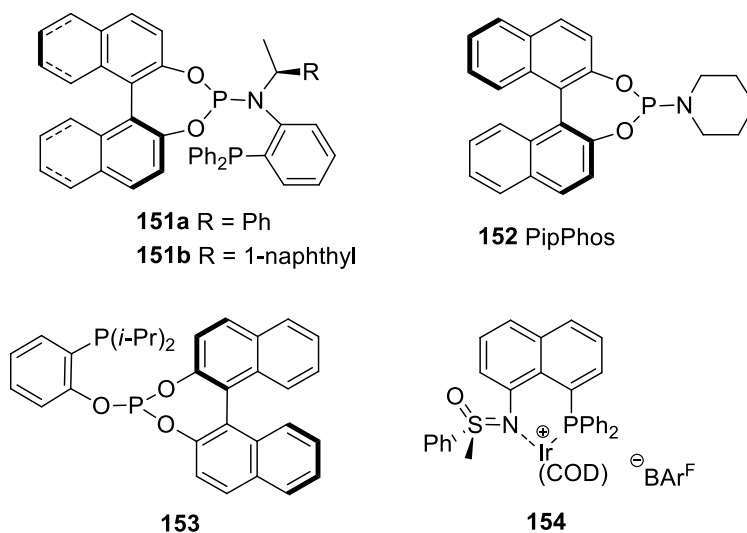
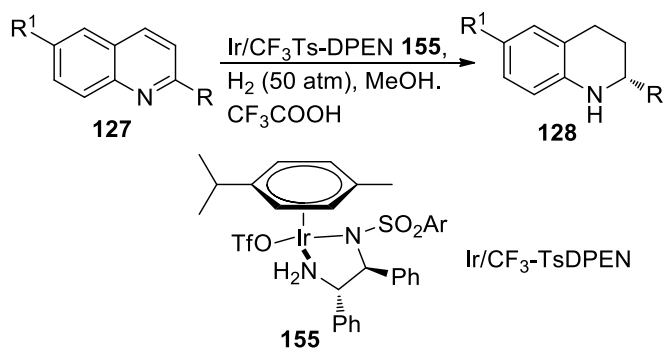


Figure 7. Phosphine-phosphoramidite and phosphine-phosphite ligands.

Another similar kind of ligand, PipPhos **152** showed enhanced stereoselectivity when chloride salts and achiral phosphine ligands were used as additives.⁹⁹ A phosphine-phosphite ligand **153** was developed by Pizzano and Vidal-Ferran group in 2010.

Phosphoric acid as additive was necessary to improve activity and enantioselectivity, while iodine had no effect on them.¹⁰⁰ Bolm and coworkers synthesized naphthalene-bridged *P,N*-type sulfoximines **154** and when applied to the asymmetric hydrogenation of quinolines, products were obtained in up to 90:10 er.¹⁰¹ Iodine, the common additive, had negative effect on this catalyst system leading to low conversions and selectivities.

Most of the ligands used in Ir-catalyzed hydrogenation have been phosphine based. An exception to this was Fan's diamine based ligand **155** which was found to react smoothly without any inert gas protection (Scheme 40).¹⁰² The products were formed in high yield with up to 99% ee at catalyst loading of 0.2 mol%.

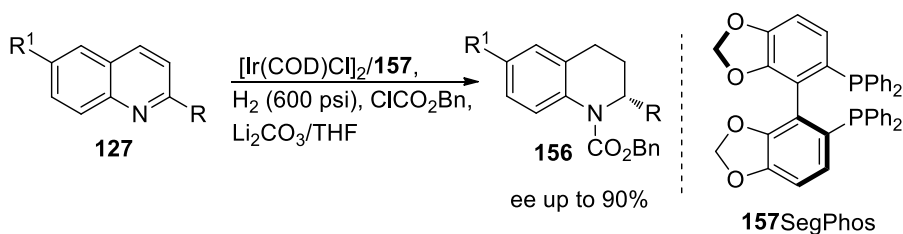


Scheme 40. Asymmetric hydrogenation of quinolines using diamine ligands.

1.2.3.7. Other Additives

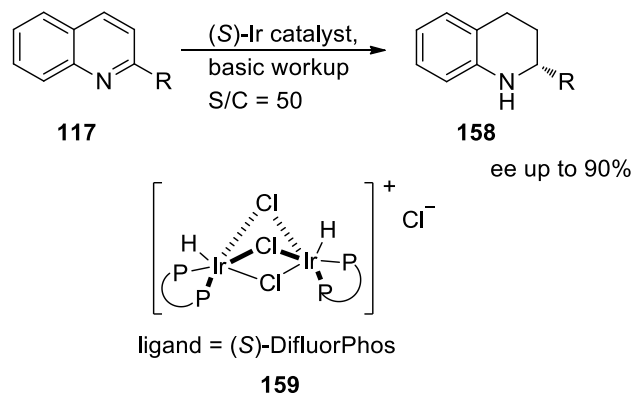
Chloroformates were also employed as additives in place of iodine. It offers a number of advantages: it can reduce the aromaticity of the ring by electron withdrawal, prevent catalyst poisoning and can act as a secondary coordination group between substrate and catalyst. The use of [Ir(COD)Cl]₂/(*S*)-SegPhos **157**/ClCO₂Bn/Li₂CO₃ catalytic system gave products with 88-90% ee (Scheme 41).¹⁰³ To avoid the additional

deprotection needed for these reactions, Brønsted acids were employed instead, where piperidine triflic acid gave the best results.¹⁰⁴



Scheme 41. Chloroformate activated asymmetric hydrogenation of quinolines.

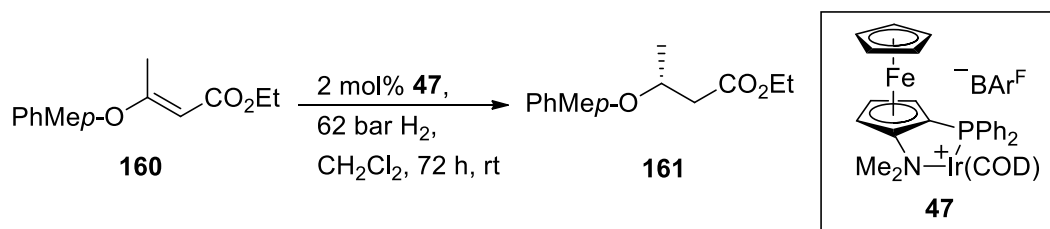
Using 2-aryl and 2-alkyl substituted quinolinium salts as substrates and cationic dinuclear triply halogen bridged iridium (III) complex **159** with axially chiral diphosphine ligand as catalytic species; asymmetric hydrogenation was carried out by Mashima and Genet *et al.* In the presence of iodine and using DifluorPhos as the ligand, 2-substituted tetrahydroquinolines were obtained up to 95% ee (Scheme 42). An unexpected preference for chloro- and bromo-iridium catalyst over iodo-iridium catalyst was observed in this case.¹⁰⁵



Scheme 42. Asymmetric hydrogenation of quinolinium salts.

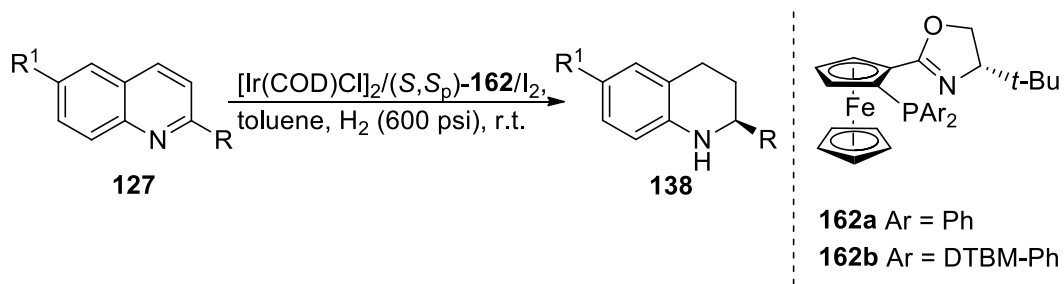
1.2.3.8. Ferrocene-Based Ligands in Asymmetric Hydrogenation

The use of planar chiral 2-phosphino-1-aminoferrocene ligands and their Ir(COD)BAr^F complexes in asymmetric hydrogenation of several prochiral alkenes were reported by the Metallinos group with enantioselectivities up to 92% (Scheme 43).¹⁰⁶ The iridium complex **47**, was found to catalyze asymmetric hydrogenation of cinnamate esters in up to 96:4 er.



Scheme 43. Asymmetric hydrogenation of alkenes with catalyst **47**.

The ferrocenyloxazoline-derived *P,N* ligand **162** was used in the iridium catalyzed asymmetric hydrogenation of 2-substituted quinolines and gave up to 92% ee with substrate/catalyst ratio up to 1000 (Scheme 44).¹⁰⁷ It was found that central chirality dominates the absolute configuration of products. Further improvement of the catalytic activity was achieved by introducing bulky functional groups on the phosphorus atom.^{95a}



Scheme 44. Iridium catalyzed asymmetric hydrogenation of substituted quinolines using ferrocenyl *P,N* ligand.

1.2.3.8. Iridium Catalyzed Hydrogenation of Quinolines Under Mild Conditions

The first report on catalytic systems using *N*-heterocyclic carbenes was reported by Crabtree *et al.*¹⁰⁸ They synthesized six different ionic complexes, Figure 8, either through base-assisted metalation¹⁰⁹ from an imidazolium salt and $[\text{Ir}(\text{COD})\text{Cl}]_2$ or by transmetalation from a silver complex,¹¹⁰ followed by the addition of a neutral ligand in the presence of a noncoordinating anion PF_6^- or $\text{BAR}^{\text{F}-}$. The benzimidazole and imidazole complexes with various wingtip substitutions thus synthesized were found to be air stable both in the solid state and in solution (Figure 8).¹¹¹ The geometry around iridium in **163a** was found to be square planar as shown by single crystal X-ray analysis.

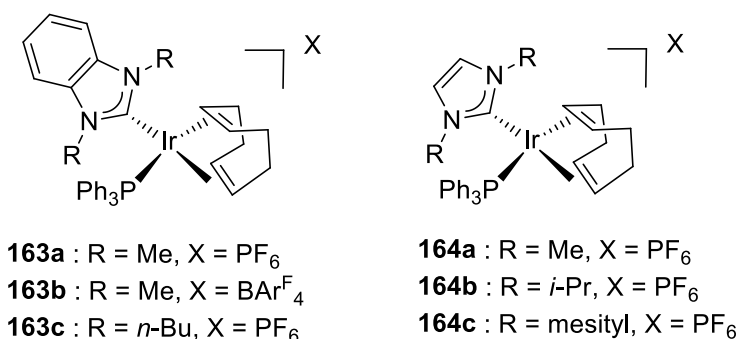
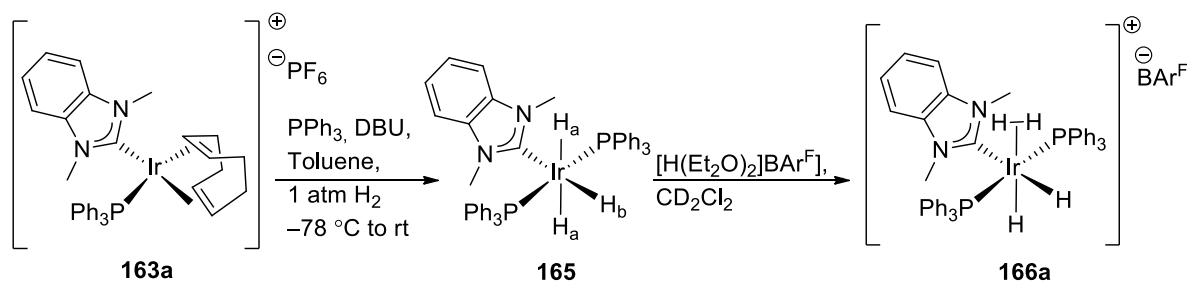


Figure 8. Iridium precursor complexes screened for catalysis.

The initial screening was done at high hydrogen pressures (70 atm) using **163a** and 2-methyl quinoline as a substrate, only trace amount of 2-methyl 1,2,3,4-tetrahydroquinoline was obtained. Upon addition of triphenylphosphine, the activity improved considerably while stoichiometric amounts of iodide did not make any change. The reaction was found to be solvent-dependant; high conversions were obtained in toluene. On catalyst screening, **163a** was found to be the best catalyst, while sterically hindered **164a-c** gave poor to no conversion. Good conversions were obtained even at 1 atm of H_2 at reasonable times (<24 h) with 1 mol % of catalyst at 35 °C.

Using the above optimized conditions, a number of 2-, 6-, 8- substituted quinolines were hydrogenated in high yields. Some sterically demanding substrates required higher hydrogen pressures (5 atm). The imine underwent hydrogenation while acetophenone was found to be completely unreactive.

To understand the mechanism of the reaction, some reactive intermediates were isolated. When **163a** was treated with PPh₃ and H₂ in presence of a noncoordinating base DBU, neutral meridional iridium trihydride species **165** was obtained (Scheme 45). The structure was confirmed by ¹H and ³¹P NMR shifts and coupling constants. The triplet of doublet at δ -11.08 ppm (H_a, $J_{\text{PH}} = 17.6$ Hz, $J_{\text{HH}} = 4.4$ Hz) and triplet of triplets at δ -13.86 ppm (H_b, $J_{\text{PH}} = 19.3$ Hz, $J_{\text{HH}} = 4.4$ Hz) were assigned to two types of hydrides. The small coupling constants indicated that these hydrides were *cis* to the phosphines and were mutually *trans*. The single peak in the ³¹P NMR spectrum further proved that the phosphines were *trans* to each other.

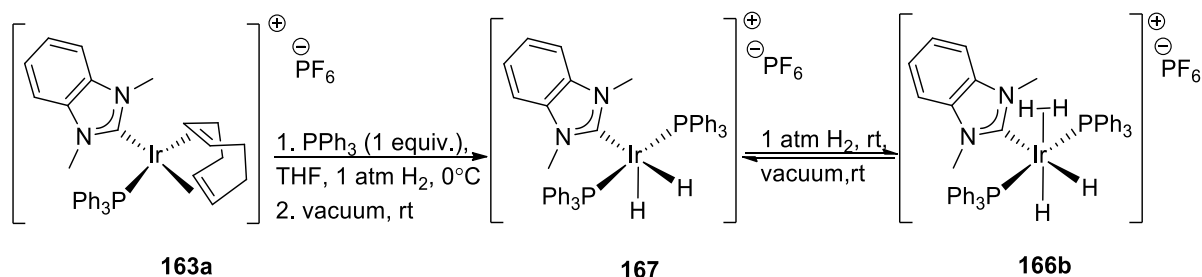


Scheme 45. Generation of iridium trihydride and dihydrogen complex.

On addition of [H(Et₂O)₂][BAr^F₄] to **165**, cationic species **166a** was formed which showed a single broad hydride resonance at δ -7.71 ppm corresponding to 4H per Ir (Scheme 45). Possible structures include a fluxional classical iridium(V) tetrahydride and a fluxional nonclassical iridium (III) dihydrogen dihydride. Variable temperature NMR

studies showed T_1 (min) value for complex **166a** was 30 ms at 233K (CD_2Cl_2) while complex **165** exhibited T_1 (min) value 350 ms at 253K (CD_2Cl_2) at 500 MHz. A nonclassical hydride signal typically exhibits a $T_1(\text{min})$ value no larger than 35 ms at 250 MHz which corresponds to 70 ms at 500 MHz.¹¹² The broad signal was assigned to the coalescence of both classical and non-classical hydrides due to rapid fluxional exchange combined with anomalous broadening.

A different hydride **167** was isolated from **163a**, PPh_3 and hydrogen without using a base. The reaction showed characteristic color changes during its formation: in the presence of hydrogen, the initial orange-red solution became colorless and a white solid precipitated; its color reappeared upon applying a vacuum (resulting in loss of hydrogen). This color change was found to be reversible; treatment of **167** with 1 atm H_2 gave **166b** the PF_6^- analogue of **166a** (Scheme 46). From X-ray crystallography and ^1H NMR data, the ionic iridium hydride **167** was found to have *cis* hydride geometry. Using variable temperature NMR experiments it was confirmed that **167** was a classical iridium dihydride complex.

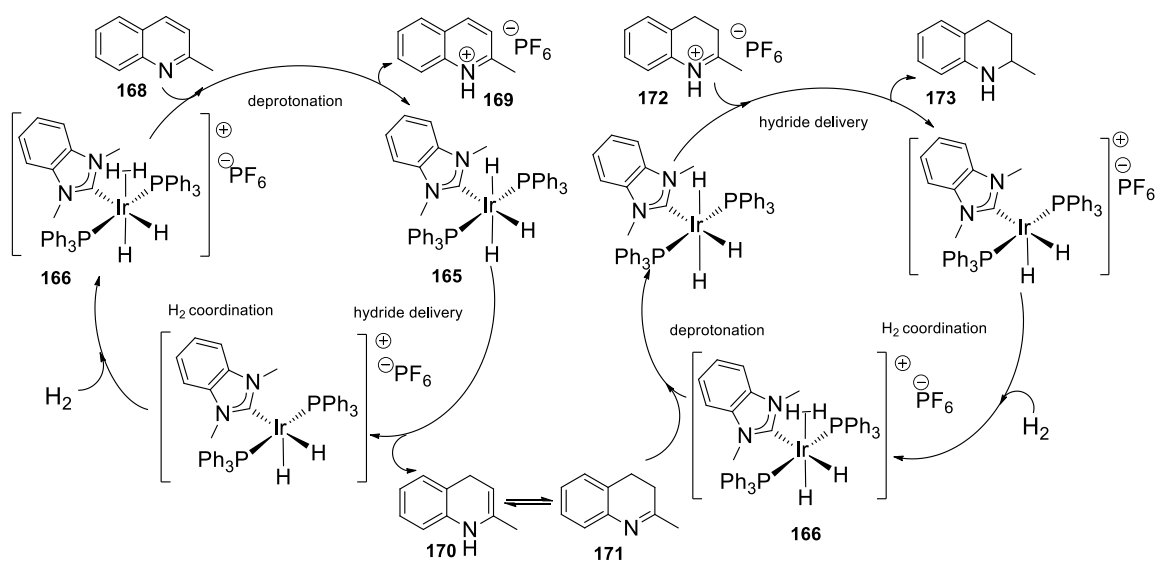


Scheme 46. Generation of iridium dihydride and dihydrogen species.

Having isolated the iridium hydride species, studies were done to establish the potential reactive intermediates in the catalytic cycle. Complex **165** by itself failed to

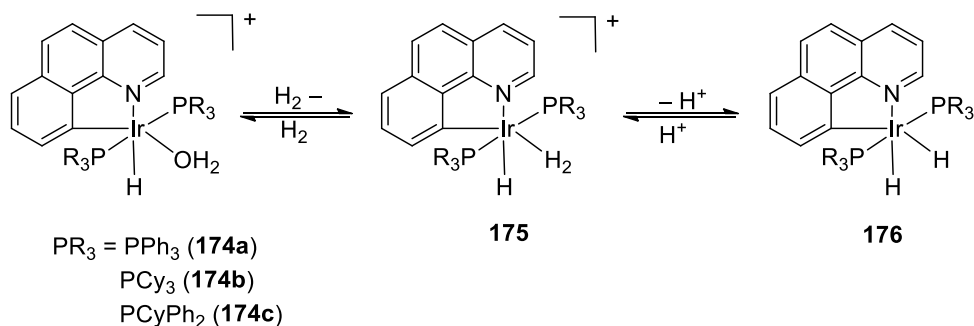
hydrogenate 2-methyl quinoline, under optimized conditions but on addition of $[\text{H}(\text{Et}_2\text{O})_2][\text{BAR}^{\text{F}}_4]$, the protonated substrate allowed hydride delivery from complex **165**. However, dihydride complex **167** was capable of delivering quinoline hydrogenation even without the acid. Hence it can be inferred that a dihydrogen complex analogous to **166** was formed *in situ* and that this acidic species then carried out stepwise proton delivery and hydride delivery to substrate.

Based on experimental studies (*vide supra*) and DFT calculations, a sequential proton and hydride transfer by invoking an outer sphere mechanism has been postulated for this reaction (Scheme 47). The cationic iridium H_2 complex (**166**) activates the substrate by protonation of quinoline nitrogen. Subsequent hydride transfer from the catalyst to the 4-position of substrate gives the enamine species (**170**). Isomerization of the 1,4-dihydroquinoline gives the 3,4-isomer (**171**) which enters another cycle of protonation and 1,2-hydride transfer to give tetrahydroquinoline.

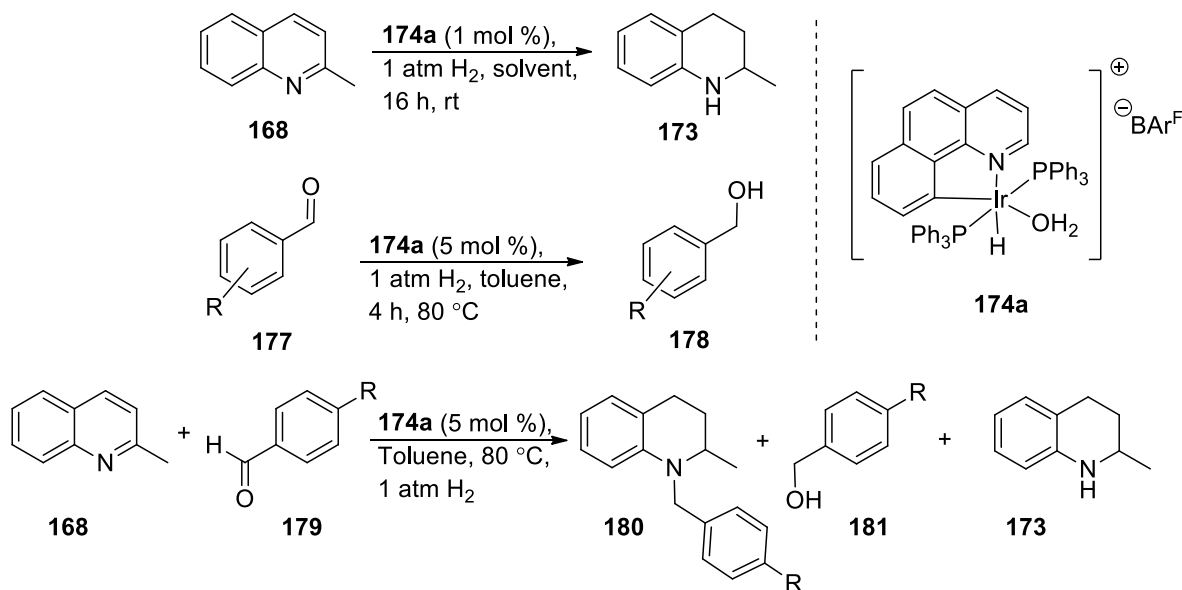


Scheme 47. Mechanism for the hydrogenation of quinolines.

Although **163a** was capable of hydrogenating a range of quinolines, it had restricted solvent scope. In search of a more efficient catalyst, Crabtree and coworkers synthesized a cyclometalated benzoquinoline complex of Ir(III)¹¹³ which was shown to add H₂ readily to give a dihydrogen complex **175**, which was shown to enter into a reversible protonation in equilibrium with **176**, similar to **166** (Scheme 48).¹¹⁴



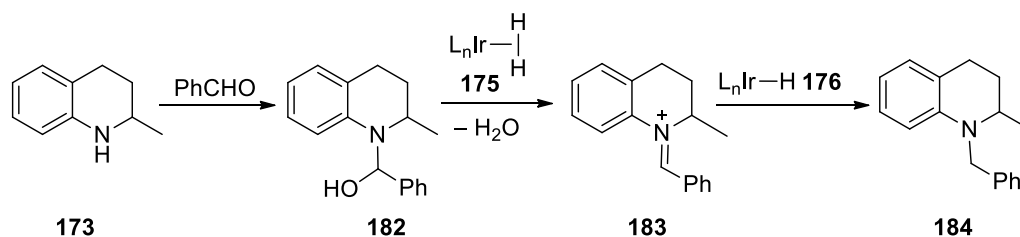
Scheme 48. Generation of dihydrogen species from **174**.



Scheme 49. Reduction and reductive alkylation using **168a**.

Catalyst screening showed that **174a** gave full conversion of quinaldine **168** with 1 mol % of catalyst under 1 atm H₂ at room temperature in a wide array of solvents including THF, 1,4-dioxane and cyclopentyl methyl ether. Further substrate scope was investigated with benzylic aldehydes. In presence of stoichiometric amounts of Hünig's base, various 2- and 4- substituted benzaldehydes were hydrogenated under 1 atm H₂ at 80 °C to afford products in high yields. Ketones and aliphatic aldehydes were unreactive under these conditions.

Crabtree and coworkers extended their studies towards one-pot, tandem reduction of quinaldine with excess benzylic aldehydes to give *N*-alkylated tetrahydroquinaldine products. The reductive alkylation was tolerant of aldehydes substituted at the 4-position with mildly electron donating and withdrawing groups. However, acetophenone and *N*-benzylidenemethylamine were unreactive to alkylation. The mechanism of the reaction involves the formation of hydrogenated heterocycle **173** which reacts with aldehyde to give hemiaminal **182**. In the presence of an acidic catalyst, a highly activated iminium species **183** is generated which then undergoes reduction to afford the product **184**.



Scheme 50. Mechanism of reductive alkylation.

2. Objectives

The aim of the current work is to develop a direct method for the synthesis of 2-substituted planar chiral ferrocenes. Since lithiation-substitution has proved to be an efficient method for the selective synthesis of ferrocenes, this approach was chosen. The advancement of this methodology would require the development of a practical *N*-based chiral auxiliary for planar chiral induction in ferrocenes.

A practical chiral auxiliary must have the following features:

- a) It must be available in large quantities from inexpensive starting materials
- b) It must be stable to the strong bases used in lithiation
- c) It must provide products in high diastereomeric ratio
- d) It should provide a means to synthesize both enantiomers of planar chiral products
- e) It must be readily converted to other functional groups, including primary amines.

Previous work in the Metallinos group has shown that BF_3 activated aminoferrocenes underwent enantioselective lithiation in presence of chiral cyclohexane diamine ligands to afford 2-substituted aminoferrocenes (Scheme 12).⁴⁵ Even though this approach proves to be feasible for the synthesis of planar chiral ferrocenes; lower enantioselectivity (up to 80% ee) and lack of manipulability make this method less desirable.

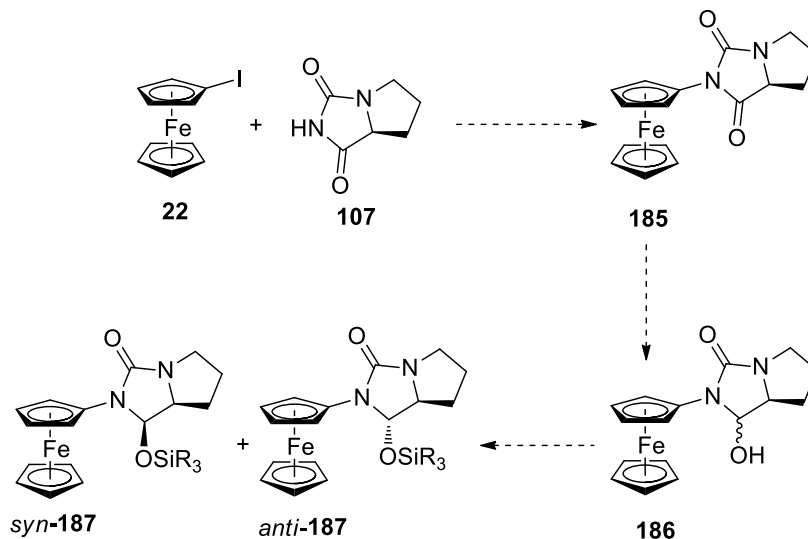
Hence a new approach was chosen, which included the use of ferrocenyl phthalimidine as a chiral auxiliary (Scheme 23).⁶⁵ When ferrocenyl phthalimidine was subjected to lithiation conditions using LDA and quenched with ClSiMe_3 , 2-silylated

product was obtained as a diastereomerically pure compound along with inseparable mixture of two aryl-silylated products. Hence it can be stated that if the phthalimidine starting material was a single stereoisomer, then Cp-silylation followed by deprotection of nitrogen to primary amine would afford product with solely planar chirality. This directing group also had the advantage of ease of manipulability using simple transformations.

The use of a chiral auxiliary derived from readily available and inexpensive L-proline was found to facilitate diastereo- as well as enantioselective lithiation reactions (Scheme 26, 27).^{69, 71} The products formed were easily converted to several other functionalities such as ligand precursors and chiral guanidines. Hence a chiral directing group derived from L-proline which satisfies the above-mentioned features of a practical chiral auxiliary would be apt for the development of a practical method for the synthesis of planar chiral ferrocenes.

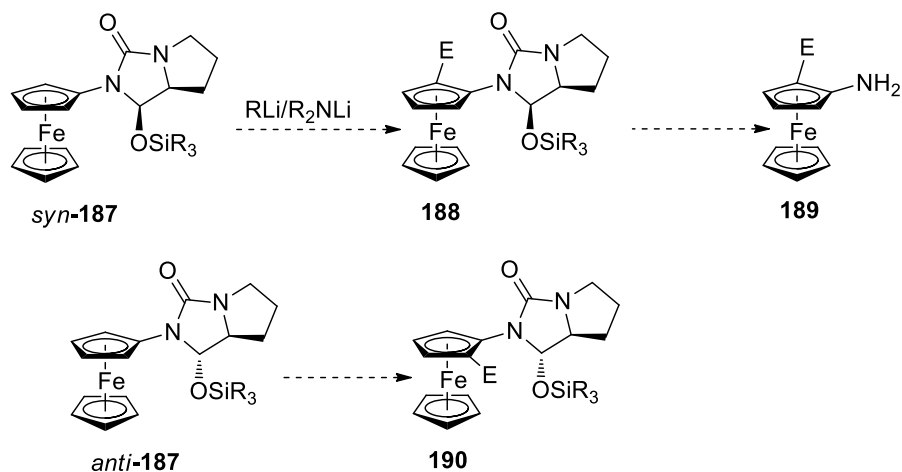
With this global objective in mind, the sub-objectives of this work are:

1. To investigate the utility of a chiral directing group prepared from the inexpensive L-proline hydantoin **107**, based on the work done on ferrocenyl phthalimidines and the demonstrated utility of proline hydantoin in diastereo- and enantioselective lithiation chemistry. The ferrocenyl hydantoin **185** may be synthesized by copper mediated coupling of iodoferrocene **22** and **107**⁶⁶ and can be reduced to corresponding hemiaminal which may require protection as *N*-silyloxy moiety to fix the stereochemistry of hemiaminal ether (Scheme 51).



Scheme 51. Proposed use of L-proline hydantoin as a removable/manipulable, *N*-based directing group.

2. To study the stereoselectivity induced by these epimers in the diastereoselective lithiation-substitution reaction. Investigate conditions that will allow manipulation of the auxiliary into other functionalities including but not limited to primary amines.



Scheme 52. Proposed diastereoselective lithiation-substitution and manipulation of chiral auxiliary.

3. To explore the utility of these compounds to act as ligand precursors to make metal complexes. These complexes will be used as catalysts for various asymmetric transformations.

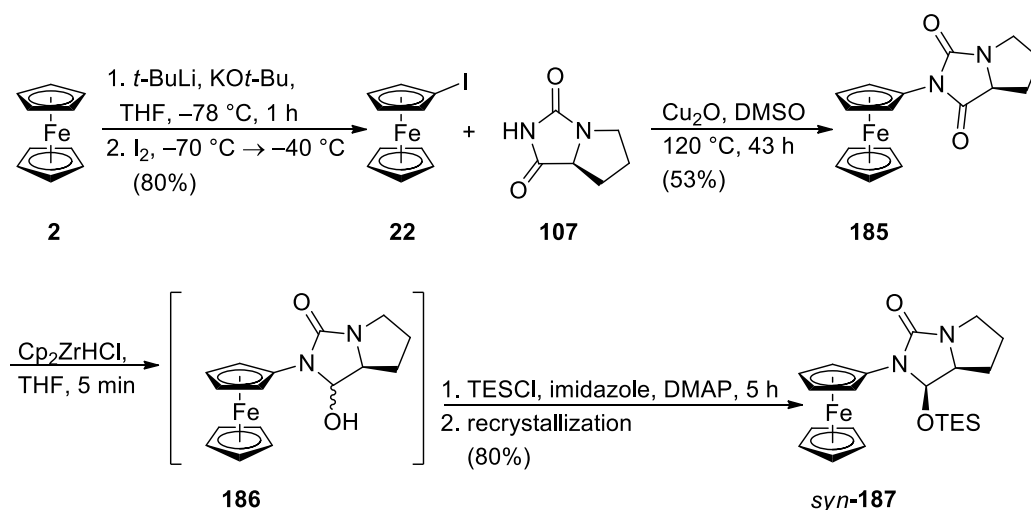
3. Results and Discussion

3.1. Diastereoselective Synthesis of Planar Chiral *N*-Substituted Ferrocenes

There are several different methods reported in the literature for the synthesis of iodoferrocene, one of the required bulk starting material for this project. Among the methods known, Kagan's procedure using *t*-BuLi and electrophile quench with *n*-Bu₃SnCl at 0 °C affords a crude mixture of 1-monosubstituted and 1,1' disubstituted stannyl ferrocenes. It requires distillation for the isolation of monosubstituted product which was then treated with molecular iodine to get iodoferrocene (Scheme 1).^{13a} Alternatively, iodoferrocene may be prepared by isolation of pyrophoric lithioferrocene which may be quenched with elemental iodine. To simplify the preparation of this key compound, a procedure reported by Mueller-Westerhoff, used to prepare formylferrocene from ferrocene devoid of 1,1'-diformylferrocene, was adapted.¹⁵ Thus, in the presence of substoichiometric amounts of KO*t*-Bu, lithioferrocene **5** was generated by *t*-BuLi lithiation. Subsequent quench with iodine gives iodoferrocene **22** in 80% yield (Scheme 53).

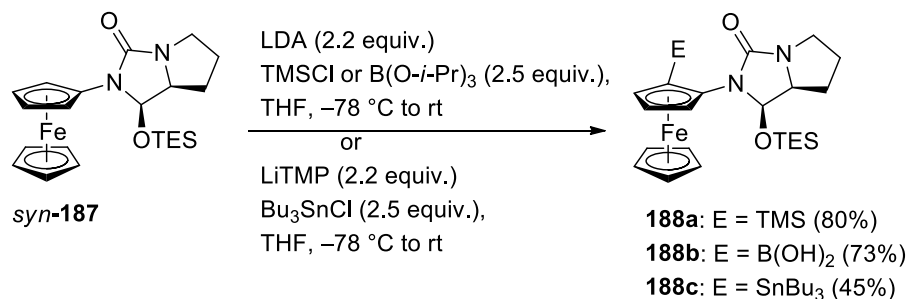
To couple iodoferrocene with L-proline hydantoin, Bildstein¹⁴ and Sato's procedure⁶⁶ [used for the synthesis of ferrocenyl phthalimide **88** (Scheme 23)], involving Cu₂O-mediated coupling, was used. This procedure afforded product **185** in good yield, but the product was found to have undergone partial racemization (scalemic, 52% ee). On screening different solvents for this reaction, CH₃CN and DMSO were found to give product in high enantiomeric purity (as measured by chiral HPLC). To minimize the reaction time, a solvent with a higher boiling point, DMSO was chosen which afforded product **185** in 53% yield.

The *N*-ferrocenyl hydantoin **185** thus obtained was then reduced using Schwartz's reagent.¹¹⁵ Schwartz's reagent has been used primarily to reduce amides to aldehydes.¹¹⁶ It was felt that reduction of hydantoin **185** with this reagent would be chemoselective in that the amide carbonyl would be reduced in preference to the urea. In addition, the purported stability of the initial aminoalkoxide intermediate offered the possibility that the silyl-protected aminal ether would be produced as a single stereoisomer if the initial hydride addition was selective. Indeed, reduction of **185** with Schwartz's reagent proceeded diastereoselectively and the product was *O*-silylated *in situ* by using chlorotriethylsilane to afford a 10:1 mixture of *syn/anti* epimers, that was recrystallized to give *syn*-**187** in 80% yield (Scheme 53). The methine hydrogen signal at δ 5.44 ppm, α to silyloxy group, was found to be a doublet with a coupling constant of 6.3 Hz, typical for *syn* stereochemistry. The hydride addition must be stereoselective and the intermediate seems to have configurational stability because when the intermediate hemiaminal was isolated, a 1:1 mixture of epimers were obtained.



Scheme 53. Synthesis of compound *syn*-**187**.

The ability of *syn*-**187** in the diastereoselective-lithiation substitution was tested in reactions with lithium amide bases using *in situ* electrophiles. When *syn*-**187** was treated with 2.2 equivalents of LDA with a mixture of either TMSCl or B(O-*i*-Pr)₃ in THF at -78 °C, products **188a-b** were isolated in good yields. The products were found to be single diastereomers by ¹H and ¹³C NMR, showing that the selectivity in deprotonation of the *ortho* Cp hydrogen was at least 95:5.¹¹⁷ This selectivity is comparable to what is obtained using other chiral directing groups such as Ugi's amine^{30b} and oxazolines.^{60b, 61b, 62a} This reaction also represents the first diastereoselective lithiation and substitution reaction using a chiral directing group which contains the challenging nitrogen-ferrocene bond already installed by design.^{52b} Similar results were obtained with stannane using LiTMP and *in situ* Bu₃SnCl under analogous conditions.



Scheme 54. Diastereoselective lithiation of *syn*-**187** with lithium amide bases.

Further proof to the selective deprotonation by LDA and formation of *S*-planar chiral (*S_p*) boronic acid was obtained by single crystal X-ray diffraction of **188b** (Figure 9). The compound crystallizes in the trigonal *P*3₂ space group as two independent molecules. The dihedral angle between the methine hydrogen α to silyloxy group and the methine of pyrrolidine ring was found to be 11.6° which is consistent with the observed 6.3 Hz coupling constant observed in the *syn*-diastereomer **187**. The cyclopentadienyl

rings were found to be slightly staggered with a torsion angle of 1.6°. Solution using the S_p enantiomer model [Flack parameter = 0.010(13)] confirmed the S -planar chirality of **188b** as expected.

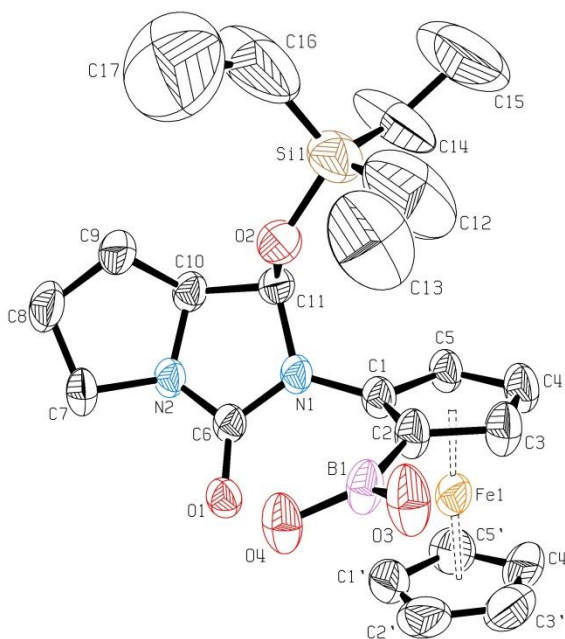
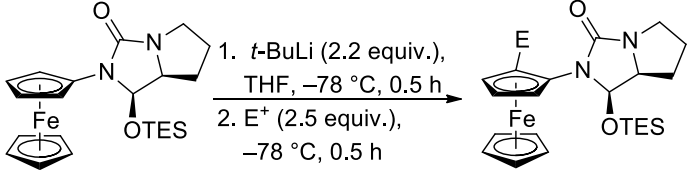


Figure 9. ORTEP depiction of **188b** with 30% probability ellipsoids (hydrogens omitted for clarity).

Encouraged by these results, the scope of the reaction was tested with alkylolithiums by using sequential diastereoselective lithiation-electrophile quench of *syn*-**187** (Table 1). In this way, electrophiles that are unstable to *in situ* deprotonation with lithium amide bases may be used. Thus lithiation of *syn*-**187** with 2.2 equivalents of *t*-BuLi at -78 °C for 30 min. in THF, followed by quench with MeI, gave the methyl adduct in 91% yield and >95:5 dr as determined by ^1H NMR. Attempts to lithiate *syn*-**187** using *n*-BuLi or *i*-PrLi gave methyl adduct **188d** as a single diastereomer, but with poor yield. Hence by using the optimized reaction conditions; various planar chiral products **188a-h** were obtained in good to excellent yields. With the exception of aldehyde (74:4

dr), all products were formed with 95:5 dr. The TMS, B(OH)₂ and SnBu₃ adducts were found to be optically and spectroscopically indistinguishable from the products obtained by deprotonation using lithium amide bases. Additionally, transmetalation of LiTMP-derived stannane with *n*-BuLi at -78 °C, followed by MeI or B(OEt)₃ quench afforded products identical to those obtained by deprotonation of *syn*-**187** with either *t*-BuLi or LDA. Moreover, the selective deprotonation of pro-*S*_p hydrogen using LDA was confirmed by the X-ray structure of boronic acid **188b**. The boronic acid **188b** obtained either by using *t*-BuLi or by transmetalation from the stannane **188c** was found to be optically and spectroscopically identical to the one obtained using LDA. This result shows that the lithiation stereochemistry of *syn*-**187** did not change upon switching from lithium amide base to *t*-BuLi. All products **188a-h** are formed *via* selective deprotonation of pro-*S*_p hydrogen irrespective of the base used. Hence by using this method, a variety of carbon as well as hetero-atom substituents could be installed selectively on the ferrocene ring.

Many of these heteroatom substituted products such as the iodide, stannane or boronic acid, may be useful for further transformations such as cross-coupling and metal-halogen exchange reactions. Unfortunately, attempts to introduce a phosphino substituent using chlorodiphenylphosphine as electrophile resulted in decomposition of the product along with partial recovery of the starting material.

			
E ⁺	E	188	Yield (%) [*]
SiMe ₃ Cl	SiMe ₃	a	84
B(OEt) ₃	B(OH) ₂	b	80
SnBu ₃ Cl	SnBu ₃	c	87
MeI	Me	d	91
ICH ₂ CH ₂ I	I	e	91
Me ₂ S ₂	SMe	f	94
Ph ₂ CO	Ph ₂ C(OH)	g	87
DMF	CHO	h	70 ^a

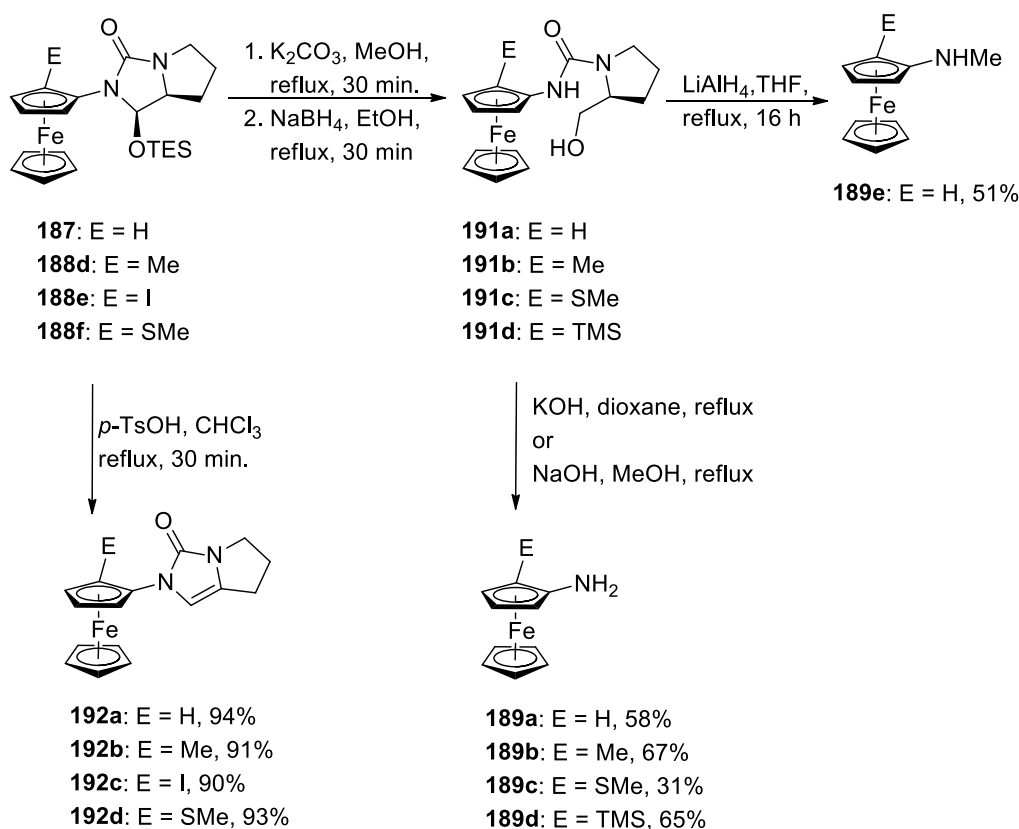
a 94.5:5.4 dr (89% de)

* isolated yields after column chromatography

Table 1. Substrate scope for lithiation of *syn*-**187**.

Having established the lithiation-substitution method, our next focus was to exploit the inherent designed lability of the *O*-silyl aminal ether in the new directing group. When *syn*-**187** was treated with *p*-TsOH, and heated to reflux for 30 minutes, rapid elimination occurred to provide ferrocenyl imidazolone **192a**; repeating the same reaction conditions with **188d-f**, Table 1, generated solely planar chiral imidazolones (Scheme 55). Chiral HPLC measurement of compounds **192b-d** against the corresponding racemic standards were found to be 100:1 er (98% ee); showing that the overall synthetic sequence gives planar chiral ferrocenyl compounds in high enantiomeric purity. Similar chiral *N*-*t*-Bu-imidazolones were shown to act as precursors to C₁-symmetric NHCs *via* their chloroimidazolium salts, thus showing future applications of these compounds in catalysis.⁶⁹

When *syn*-**187** was treated with a base instead of acid (K_2CO_3 in refluxing MeOH), *O*-desilylation occurred to give the hemiaminal, which was reduced with $NaBH_4$ in EtOH.⁶⁸ The ring opened urea thus obtained was reduced with $LiAlH_4$ ¹¹⁸ in refluxing THF to afford *N*-methyl aminoferrocene **189e**. Hydrolysis of **191a** with 50% NaOH in MeOH provided aminoferrocene **189a** in 58% yield. Ultimately, this procedure was carried out on three derivatives **191b-d** to afford planar chiral 2-substituted aminoferrocenes **189b-d** in 31-67% yield.

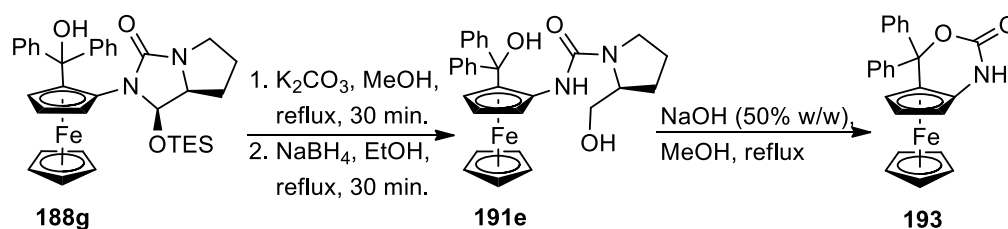


Scheme 55. Manipulation and hydrolysis of chiral auxiliary.

Initial attempt to hydrolyze urea **191d** with the aforementioned procedure provided 2-trimethylsilyl aminoferrocene **189d** only in 22% yield. Lipshutz and co-workers have shown effective hydrolysis of urea with KOH in dioxane/water.¹¹⁹ In our hand, a

modified procedure of Lipshutz's protocol (KOH in dioxane), provided clean product **189d** resulting in 65% yield. Even though products were obtained only in moderate yields, the majority of unreacted urea could be recovered in all three cases (**191b**-20% , **191c**-52% and **191d**-15%). The absolute configuration of **189b** was assigned to be S_p , by comparing its specific rotation ($[\alpha]_D^{20} -39.3$) to that of known R_p enantiomer ($[\alpha]_D^{20} +40$).^{52b, 120} This result was expected based on the X-ray structure of the boronic acid adduct **188b**.

When the benzophenone adduct was subjected to the same deprotection-reduction sequence (Scheme 56), urea **191e** was obtained which upon hydrolysis gave the corresponding oxazin-2-one **193**.

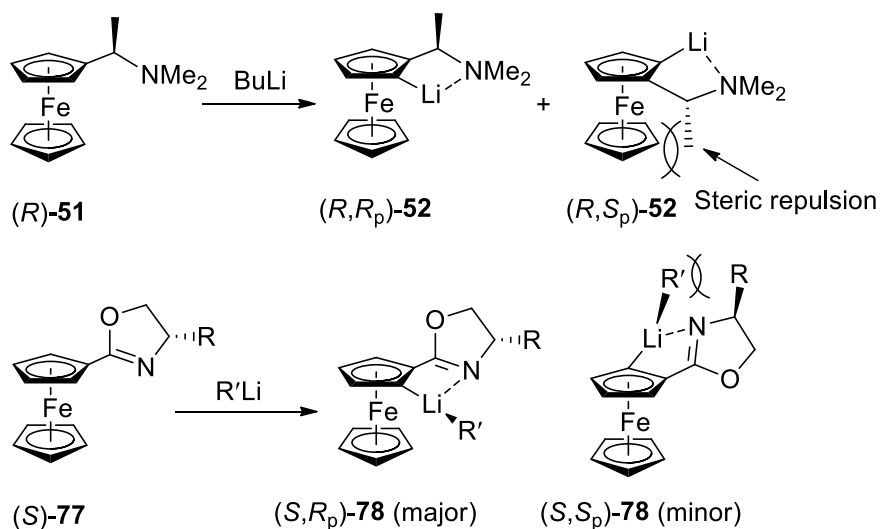


Scheme 56. Formation of oxazinone from benzophenone adduct.

3.2. On the Origin of Stereoselectivity

From the work on ferrocenyl phthalimidines, it is clear that the β -silyloxy moiety plays a vital role in determining the stereoselectivity (Scheme 23). Hence it was of interest to study the origin of stereoselectivity of *syn*-**187**. The origin of stereoselectivity in diastereoselective lithiation of ferrocenes with other chiral directing groups may be classified as one of the two cases: (a) Cp ring controlled or, (b) base controlled. In other words, lithiation selectivity is controlled primarily by the avoidance of steric interactions from either the directing group and the ferrocene core, or the directing group and the base

used for deprotonation.¹²¹ For example, in the case of Ugi's amine, lithiation is directed towards pro- R_p position selectively because the alternate conformation is disfavored by collision of the α -methyl group with the lower unsubstituted cyclopentadienyl (Cp) ring. In the case of oxazolines, deprotonation of the pro- R_p hydrogen is preferred since the alternate orientation of the directing group produces pronounced steric interactions with the base (Scheme 57).

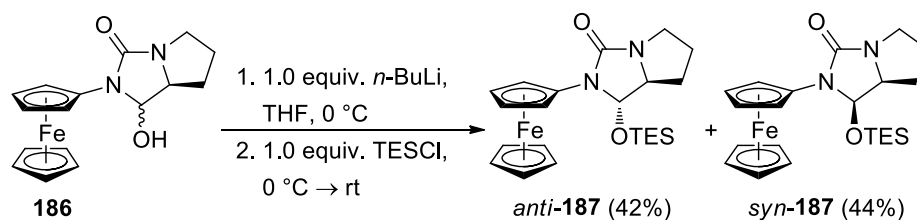


Scheme 57. The origin of stereochemistry of Ugi's amine and oxazolines.

In general, directing groups with stereogenic centers α to the ferrocene core appear to undergo Cp ring controlled lithiation (Ugi's amine or sulfoxides). Directing groups with more distant γ -ferrocenyl stereocenters (oxazolines) undergo base controlled lithiation. The directing group, *syn*-**187** has β,γ -stereogenic centers and its lithiation selectivity was found to be insensitive to the size of the base used for deprotonation (LDA, LiTMP, *n*-BuLi, *i*-PrLi or *t*-BuLi).¹²² Furthermore, the high diastereoselectivity observed for lithiation of racemic phthalimidine **90**, which has only a β -chiral stereocenter; suggest that the β position in the *syn*-**187** is more important to the reaction

outcome. In that case, it is the proximal and relatively bulky β -silyloxy moiety that plays a predominant role in the selective abstraction of pro- S_p proton compared to the γ -stereocenter of the pyrrolidine ring. To have a better insight into this, the β -epimer of *syn*-**187** (*anti*-**187**) was synthesized to determine whether it will induce the pro- R_p , rather than pro- S_p lithiation.

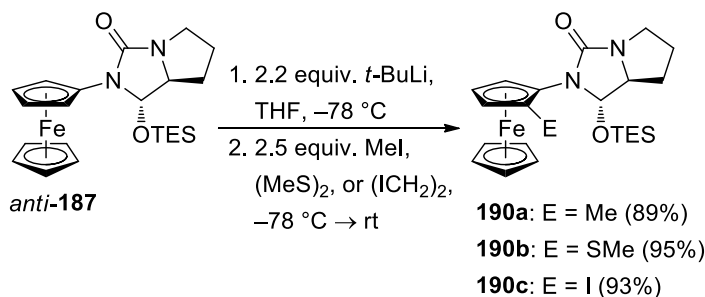
The synthesis of *anti*-**187** involved the isolation of a 1:1 mixture of hemiaminals **186**, after reduction with Schwartz's reagent. The epimers thus obtained were treated with *n*-BuLi at 0 °C to generate aminoalkoxides which were *O*-silylated with TESCl (Scheme 58). It was important to take the hemiaminals into the next step within an hour since more time resulted in the predominant formation of a *syn* diastereomer. The *syn* and *anti* diastereomers were separated *via* flash column chromatography followed by recrystallization to give *anti*-**187** and *syn*-**187** in 42% and 44% yield respectively. In the ^1H NMR spectrum of *anti*-**187**, the methine proton at δ 5.39, α to silyloxy group, was found to be a singlet showing that it may be orthogonal to the methine hydrogen of the pyrrolidine ring.



Scheme 58. Synthesis of compound *anti*-**187**.

The same lithiation conditions used for *syn*-**187** were applied for *anti*-**187** to determine the lithiation selectivity. Thus with 2.2 equivalents of *t*-BuLi in THF at -78 °C

and quenching with iodomethane gave **190a** as a single diastereomer by ^1H and ^{13}C NMR data (Scheme 59).



Scheme 59. Diastereoselective lithiation of compound *anti*-**187**.

The proof that *anti*-**187** had directed lithiation of the pro- R_p hydrogen was provided by X-ray analysis of the methyl-substituted product **190a** (Figure 10). The compound crystallizes in the orthorhombic $P2_12_12_1$ space group. The dihedral angle between the methine hydrogen α to silyloxy group and the methine hydrogen of the pyrrolidine ring was found to be 96° which is consistent with the observed singlet in the *anti*-diastereomer **187**. The cyclopentadienyl rings were found to be staggered with a torsion angle of 24° . Solution using the R_p enantiomer model [Flack parameter = 0.021(7)] confirmed the R -planar chirality of **190a** as expected.

The reaction was repeated with iodoethane and dimethyl disulphide as electrophiles, and in all cases, the products were formed in >95:5 diastereomeric ratio. When *i*-PrLi or *n*-BuLi were used instead, the degree of diastereoselectivity remained the same, but there was a decrease in conversion.

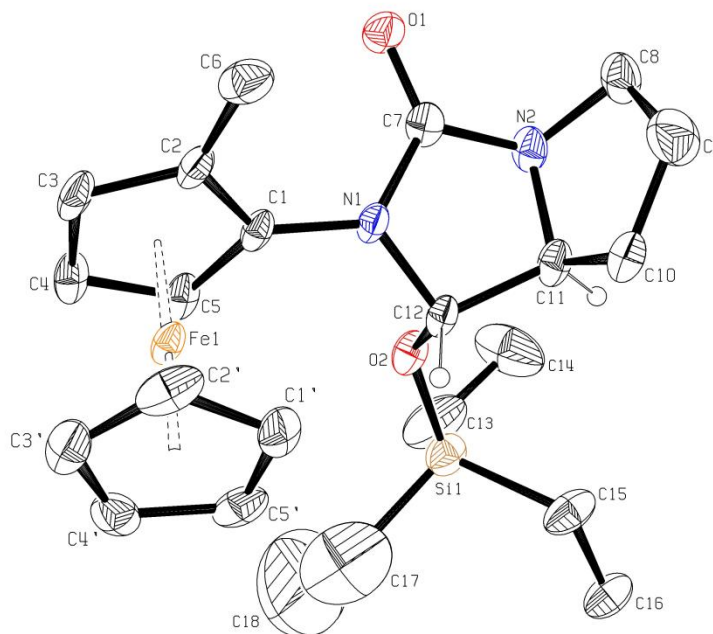


Figure 10. ORTEP depiction of (1*S*,7*S*,*R_p*)-**190a** at 30% probability. All hydrogens except H11 and H12 are omitted for clarity.

Further confirmation to the extent of planar chiral induction was obtained by synthesis of 2-substituted imidazolones by acid-induced elimination of **190a-c**. When these compounds were treated with *p*-toluenesulfonic acid in CHCl₃ at reflux for 30 min., the imidazolones **192a-c** were formed in high yields ranging from 85-95%. The products thus obtained were found to be the antipodes of the imidazolones derived from *syn* **188a-c** as observed from specific rotation and chiral stationary phase HPLC analysis. From all these observations described above, it is clear that it is the configuration of silyloxy-containing β-ferrocenyl stereogenic center of each substrate that determines the sense of planar chiral induction.

188a-c **192a-c**

ent-192a-c **190a-c**

E	yield, %	er (% ee)	[α] _D ²⁰
Me	91	99:1 (98)	−29.2
SMe	93	98:2 (96)	−129
I	90	99:1 (98)	−38.9

E	yield, %	er (% ee)	[α] _D ²⁰
Me	95	97:3 (94)	+31.0
SMe	92	95.5:4.5 (91)	+136
I	85	99:1 (98)	+40.3

Table 2. Comparison of imidazolone antipodes.

3.2.1. Spectroscopic Analysis of *syn/anti*-187 and Their Deuterated Congeners.

From the experimental results, it may be inferred that the β-silyloxy stereocenter in each substrate exerts a conformational bias making the urea carbonyl to point towards either the pro-*S_p* or pro-*R_p* hydrogens. Hence it is reasonable to assume that the lithiation occurred *via* coordination of the base to the more electron rich urea oxygen rather than the bulkier silyloxy moiety of the directing group. Further evidence of the preferred orientation of the urea carbonyl moiety was obtained by nOe difference spectra acquired by selective irradiation of the respective β-silyloxy methine hydrogens in *syn*- and *anti*-**187**. In the case of *syn*-**187**, irradiation of methine doublet at δ 5.44 produced a 1.7% nOe for the neighbouring pyrrolidine methine at δ 3.93, along with a 1.0% nOe for a Cp ring hydrogen at δ 4.30 (Figure 11). Among the other three Cp hydrogens, the most deshielded hydrogen at δ 4.80 was tentatively assigned as the pro-*S_p* hydrogen.

Similarly, in the case of *anti*-**187**, irradiation of the β-silyloxy methine at δ 5.41 produced 1.4% nOe for the Cp ring hydrogen at δ 4.46 along with a 0.6% nOe for the Cp ring proton at δ 4.97 ppm (Figure 11). The most deshielded Cp ring hydrogen at δ 4.97

having smaller nOe from the β -silyloxy methine at δ 5.41 was tentatively assigned as the pro- R_p hydrogen.

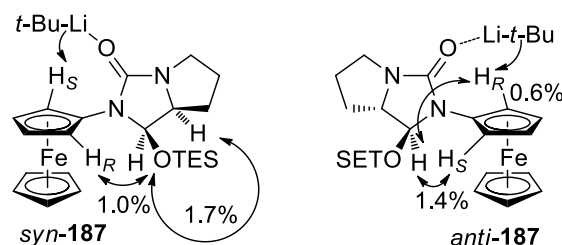
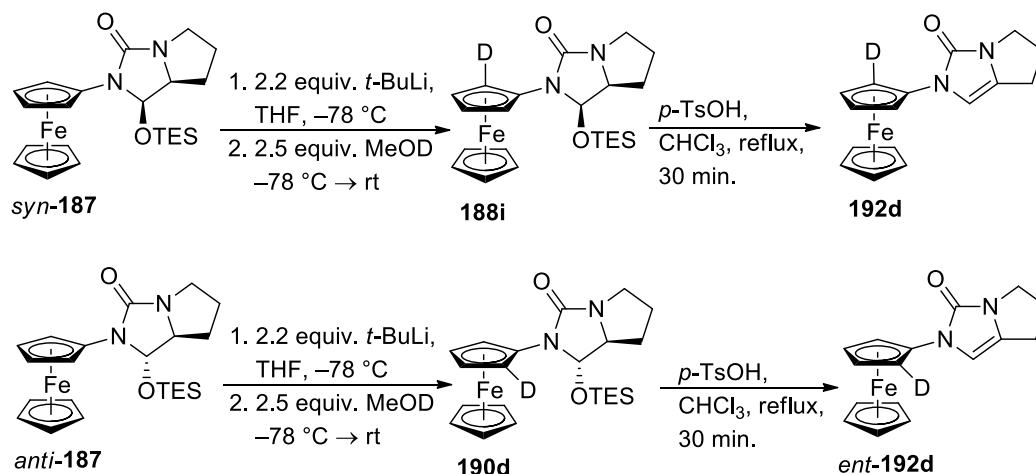


Figure 11. Relationship of key nOe's to observed sites of lithiation-deuteration for *syn*- and *anti*-**187**.

To support the above assignments, lithiation-deuteration experiments were carried out on *syn*- and *anti*- **187**. In the case of *syn*-**187**, it was expected that the signal assigned as the pro- R_p *ortho* Cp hydrogen at δ 4.30 ppm should remain as such and the signal at δ 4.80 assigned as the pro- S_p hydrogen should disappear. In accordance with these, lithiation of *syn*-**187** under standard conditions followed by addition of excess methanol- d_4 afforded a ^1H NMR spectrum of *syn*-**188i** in which the signal at δ 4.80 disappeared (Scheme 60). The integral ratio to the signal at δ 4.80 versus δ 4.30 was found to be 0.08:1. The lithiation-deuteration experiment on *anti*-**187** showed disappearance of the signal at δ 4.97 ppm with a resulting integral ratio of 0.02:1 versus the peak at δ 4.46 ppm. Subjecting these compounds to elimination conditions, imidazolones (**192d**, *ent*-**192d**) with solely planar chirality due to the presence of a deuterium as a substituent were obtained.



Scheme 60. Synthesis of deuterated antipodes.

3.2.2. Computational Modeling of *syn/anti* Lithiation.

When *syn*-**187** and *anti*-**187** were subjected to variable temperature ^1H -NMR (300 MHz) in $\text{DMSO-}d_6$ at 130 $^\circ\text{C}$, neither epimer showed any signs of signal coalescence in their respective ^1H -NMR spectra, even for Cp hydrogens *ortho* to the directing group. Additionally, the fact that both epimers showed significant nOe for *ortho*-Cp protons by irradiation of their β -silyloxy methine hydrogens suggested a large rotational barrier, or at least a conformational preference about the Cp-nitrogen bond for each substrate. To get more information about their conformational behaviour, global minima were calculated for both epimers at the B3LYP¹²³/6-31G(d,p) level of theory using Gaussian '09.¹²⁴ The lowest energy minima obtained by this process for each epimer are given in Figure 12.

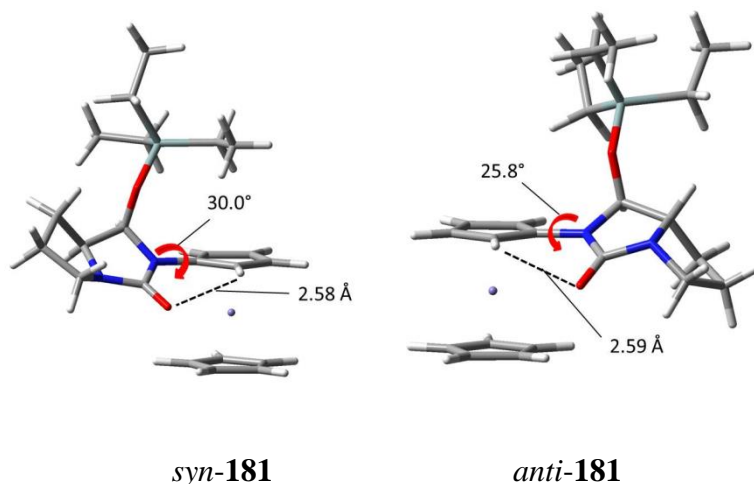


Figure 12. Calculated ground states for *syn*- and *anti*-**187**.

In both calculated global minima, the triethylsilyloxy moiety was placed well above the plane of the top Cp ring, to minimize steric interactions with the ferrocene core. The carbonyl group in the case of *syn*-**187** was found to produce a dihedral angle (carbonyl-nitrogen-Cp_(ipso)-Cp_(ortho)) of 30.0° below the plane of the substituted (top) Cp ring, i.e., pointing towards the pro-*S*_p Cp hydrogen. The contact distance between urea oxygen and pro-*S*_p Cp hydrogen was found to be 2.58 Å. Likewise for *anti*-**187**, the urea carbonyl points in the direction of the pro-*R*_p hydrogen producing a dihedral angle of 25.8°. The contact distance between the urea and the pro-*R*_p hydrogen was 2.59 Å. More information about the rotational barriers of both epimers about their Cp_(ipso)-N bonds was obtained by performing optimizations constrained about the carbonyl-nitrogen-Cp_(ipso)-Cp_(ortho) dihedral at 10° increments over a complete range of 360°. From these calculations, the overall approximate rotational barrier was found to be 16 and 10 kcal/mol for *syn*- and *anti*-**187**, respectively. From spectroscopic observations, it appeared that the real rotational barriers for each epimer may be >20.9 kcal/mol.¹²⁵ The

calculated values for rotational barriers may be an underestimation since the minimizations were done in 10° increments.

Calculations of the transition states for lithiation were done at the MP2/6-31G(d,p)//B3LYP/6-31G(d,p) level of theory using the above-mentioned conformational minima, *syn*- and *anti*-**187**, as a starting point. The transition state model predicted that the lithium of the *t*-BuLi base coordinates to the urea oxygen in such a way that the incoming carbanion is essentially coplanar with the prochiral C-H bonds of each compound (Figure 13 of *syn*-**187**). The carbonyl-nitrogen-Cp_(ipso)-Cp_(ortho) dihedral angle is tilted 45.3° below the plane of the top Cp ring to accommodate the base, an increase of 15.3° from the calculated ground state. In the case of TS-*anti*-**187**, the carbonyl group lies 41.5° below the plane of the top Cp ring with an increase of 15.7° from *anti*-**187** (Figure 13). For both epimers, the transition states of lithiation seems to avoid any significant steric interactions between the base and any parts of the directing group, which supports the hypothesis of a Cp ring controlled lithiation. The activation energies for TS-*syn*-**187** and TS-*anti*-**187** (8.8 and 6.7 kcal/mol respectively) were found to be lower than the computationally approximated rotational barriers. It may be concluded that a conformational preference, determined primarily by the β-silyloxy moiety, is responsible for the observed lithiation selectivity. Since it affects the position of urea carbonyl to point towards one of the two *ortho*-Cp hydrogens. Hence, a strong conformational preference appears to have significant influence on the stereoselectivity in these cases compared to energetically less demanding activation barriers.

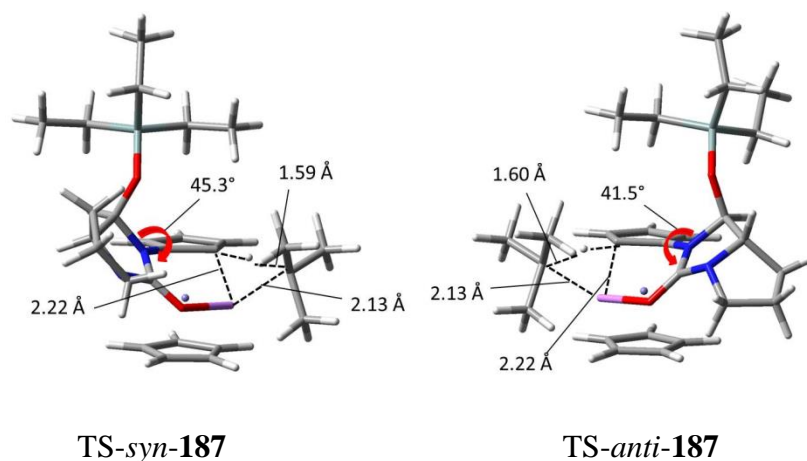
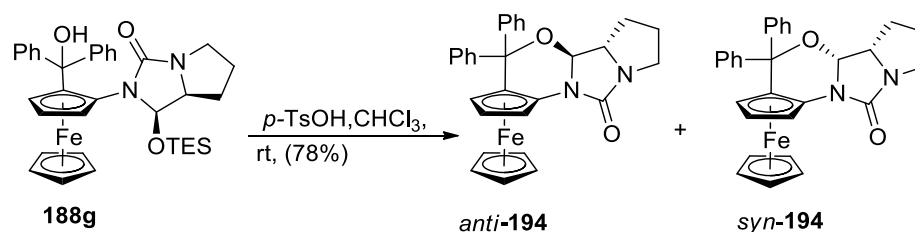


Figure 13. Single-point MP2/6-31G(d,p)//B3LYP/6-31G(d,p) calculated transition states for *t*-BuLi-mediated lithiation of *syn*- and *anti*-**187** with *t*-BuLi.

3.3. Synthesis of an Annulated Chiral *N*-Ferrocenyl Imidazolium Salt and its Ir(I) Complexes

Having established a new method for the synthesis of planar chiral *N*-substituted ferrocenes, attention turned to potential applications of any derived ligands in catalytic asymmetric reactions. A potential entry into such systems was found when alcohol **188g** underwent cyclization to give products *anti*- and *syn*-**194** (4:1 ratio) rather than elimination to the imidazolones. Repetition of this experiment on a larger scale (1.2 g) offered only *anti*-**194**, presumably because of the reversibility of the reaction by virtue of an iminium intermediate.



Scheme 61. Synthesis of annulated ureas from benzophenone adduct.

As before, the assignment of relative stereochemistry was obtained by nOe difference spectra by selective irradiation of the respective methine hydrogens α to oxygen and by coupling constants. In the case of *syn*-**194**, the methine signal at δ 4.93 ppm was found to be a doublet with coupling constant of 7.5 Hz close to other products with established *syn*-stereochemistry (eg. **188b**). Irradiation of methine doublet of *syn*-**194** at δ 4.88 introduced a 4.4% nOe for the neighbouring pyrrolidine methine at δ 3.97, along with a 1.4% nOe for a phenyl ring hydrogen at δ 7.18 (Figure 14).

In the case of *anti*-**194**, the methine signal at δ 5.46 was found to be a singlet similar to other products with established *anti*-stereochemistry (eg. **190a**) indicating 90° dihedral angle. Irradiation of the methine singlet of *anti*-**194** at δ 5.48 produced 1.3% nOe for the neighbouring pyrrolidine methine at δ 3.90 along with a 1.9% nOe for the Cp ring proton at δ 3.72 ppm, 2.2% nOe at the methylene hydrogen at δ 1.57, and 3.2% nOe for one of phenyl ring protons at δ 7.76 ppm (Figure 14).

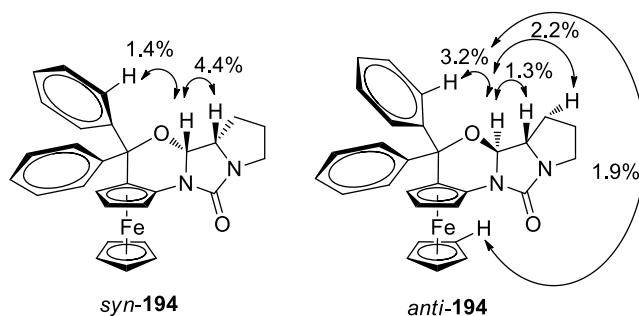
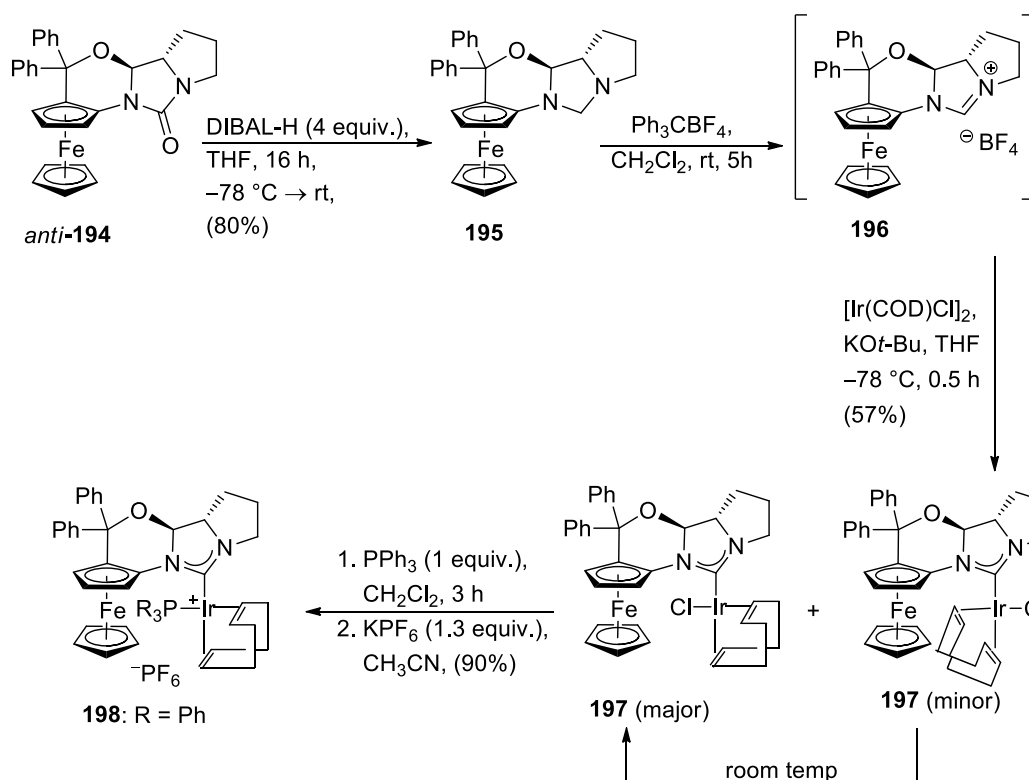


Figure 14. Key nOes of *syn* and *anti*-**194** ureas.

When *anti*-**194** was treated with four equivalents of DIBAL-H, aminal **195** was obtained (Scheme 62). The aminal was found to be isolable and indefinitely stable in a freezer at -20 °C under inert atmosphere. Subsequent oxidation of **195** with tritylium

tetrafluoroborate gave imidazolinium salt **196** which was not isolated due to its instability. Deprotonation of the imidazolinium salt with $\text{KO}t\text{-Bu}$ generated the imidazolylidene, which was trapped with $[\text{Ir}(\text{COD})\text{Cl}]_2$ to give **197** as a mixture of major and minor coordination isomers. It was found that stirring a mixture of these isomers at room temperature for 16 h led to the conversion of the minor isomer to the major isomer.



Scheme 62. Synthesis of an annulated chiral *N*-ferrocenyl imidazolinium salt and complexation to Ir(I).

Evidence for the coordination of ligand to iridium metal was obtained initially by ^{13}C NMR where a characteristic ylidene carbon signal was found at δ 206 ppm. Further confirmation on the structure was obtained by single crystal X-ray structure of **197** (Figure 15). Thus by treating a solution of **197** in CH_2Cl_2 containing one equivalent of

PPh₃ gave the cationic Ir(I) complex **198** isolated as PF₆[−] salt. This compound showed two peaks in its ³¹P NMR spectrum, a singlet at 16 ppm corresponding to the phosphine and a septet at −144.2 ppm corresponding to PF₆[−] salt.

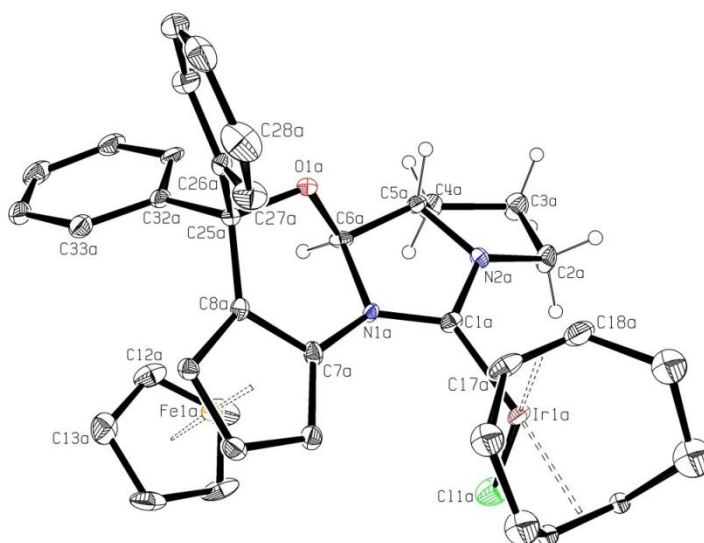
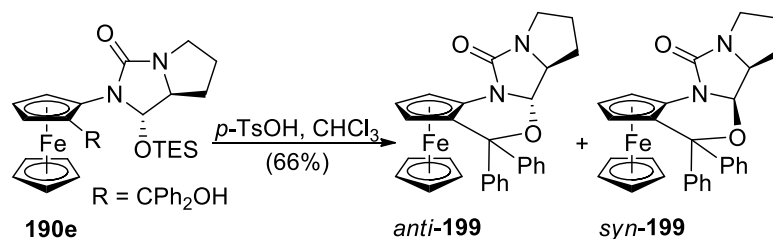


Figure 15. ORTEP depiction of **197** with 30% probability ellipsoids
(all hydrogens except H6a, H5a, H4a, H3a and H2a are omitted for clarity).

The complex crystallized in the triclinic *P1* space group as two independent molecules. The first molecule was found to have disorder in the pyrrolidine ring and the other had disorder in cyclooctadiene, which were modelled. The crystal structure shows the *anti*-stereochemistry of **197** at the C6a and C5a positions. The complex was found to be four coordinate with square-planar geometry at iridium, with a bond distance of 2.00 Å between carbenoid carbon and iridium. The cyclopentadienyl rings were found to be eclipsed and the dihedral angle between N2a-C1a-Ir1a-Cl1a was found to be 98.6(3)° avoiding steric interaction of ligand with cyclooctadiene.¹²⁶

The same synthetic pathway was used for the synthesis of an Ir(I) complex **202**, prepared from *anti*-**187** as the starting material. Diastereoselective lithiation followed by benzophenone quench gave **190e** as a single diastereomer that, on acid-mediated cyclization, gave a mixture of *syn*-**199** and *anti*-**199** ureas which were separated by column chromatography (Scheme 63).



Scheme 63. Synthesis of annulated ureas using compound **190e**.

The stereochemical assignment was obtained by the nOe difference spectroscopy acquired by selective irradiation of the respective methine hydrogen α to oxygen and 3J coupling constants. In the case of *syn*-**199**, the methine signal at δ 5.58 was found to be a doublet with a coupling constant of 6.6 Hz. This observation is in accordance with the coupling constant value seen in the case of boronic acid with *syn* stereochemistry, **188b**. For further support, nOe experiments were carried out.

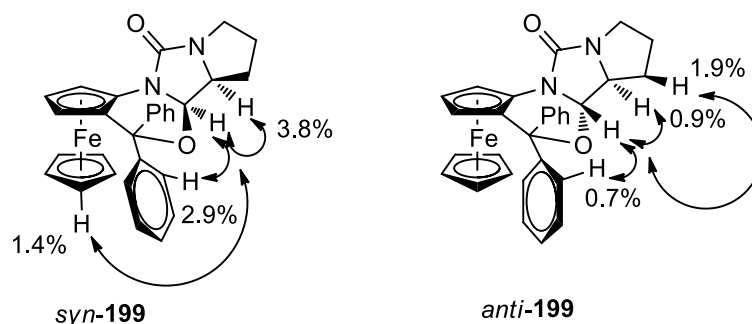
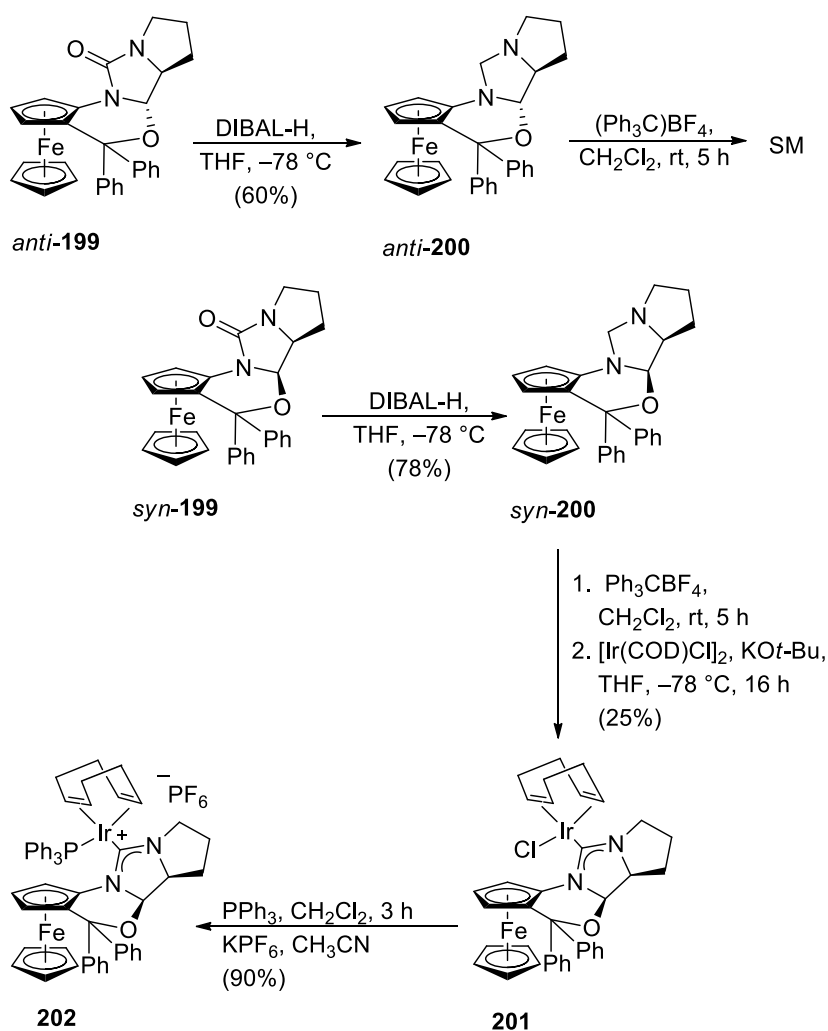


Figure 16. Key nOes of *syn*-**199** and *anti*-**199** ureas.

Irradiation of methine doublet at δ 5.60 introduced a 3.8% nOe for the neighbouring pyrrolidine methine at δ 4.21, along with a 2.9% nOe for a phenyl ring hydrogen at δ 7.75 and a 1.4% nOe for one of Cp ring hydrogens at 3.77 ppm (Figure 16). Similarly, in the case of *anti*-**199**, the methine signal at δ 4.60 was found to be a doublet with a coupling constant of 1.5 Hz. This is typical for a compound with *anti* stereochemistry (eg. *anti*-**190a**). For further evidence, irradiation of the methine singlet α to oxygen at δ 4.64 was carried out. It produced a 0.9% nOe for the neighbouring pyrrolidine methine at δ 4.01, along with a 0.7% nOe for one of phenyl ring protons at δ 7.21 ppm and a 1.9% nOe for one of methylene hydrogens of pyrrolidine ring. (Figure 16).

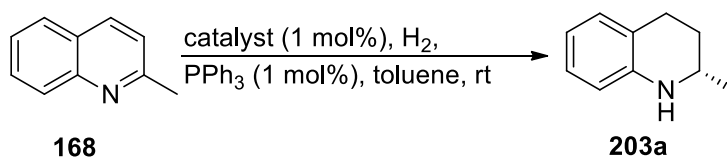
Reduction of *syn*- and *anti*-**199** gave *syn*-**200** (78%) and *anti*-**200** (60%), respectively. Among the amins, only *syn*-**200** underwent oxidation and was trapped as an iridium complex **201**. This neutral iridium complex was converted to Ir(I) complex **202** by treating its CH₂Cl₂ solution with PPh₃ followed by anionic exchange (Scheme 64).



Scheme 64. Synthesis of Ir(I) complex derived from *anti*-187.

3.3.1. Asymmetric Hydrogenation of Quinolines

Based on the work by Crabtree and coworkers, where *N*-heterocyclic carbenes (NHCs) were employed as ancillary ligands for the first time in quinoline hydrogenations,¹⁰⁸ the reactivity of complexes (**198** and **202**) in carrying out asymmetric hydrogenation being tested with 2-methyl quinoline.



Complex	Pressure	Time	er (S:R)	Yield (%)
198	45 atm	6 h	70:30	91
198	5 atm	6 h	79:21	94
198	1 atm	16 h	73:27	56
202	45 atm	16 h	68:32	84

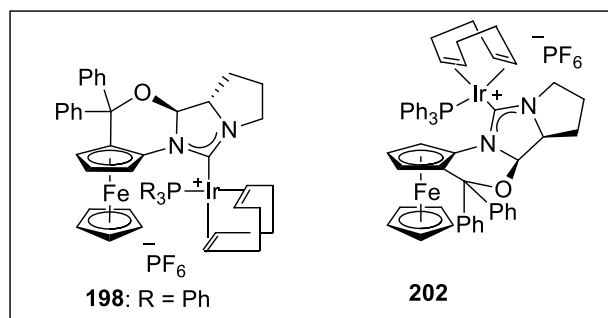
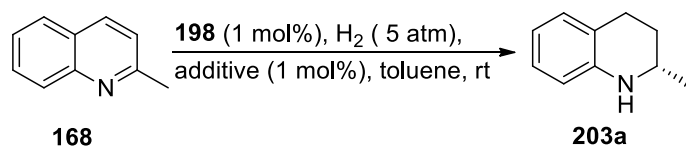


Table 3. Screening of iridium precursors for asymmetric hydrogenation.

Initial screens at high hydrogen pressures (45 atm) in toluene at room temperature (Table 3) using 1 mol% of catalyst **198** and 1 mol% PPh₃ as an additive gave full conversion in 40% ee. When reaction was repeated at 5 atm of hydrogen, full conversion to 2-methyl tetrahydroquinoline **203a** was observed in 79:21 er (58% ee). Surprisingly, lower selectivity (46% ee) and slower conversion was observed when the reaction was carried out in 1 atm of H₂ due to prolonged reaction time which can lead to decrease in selectivity due to racemization. Complex **202**, derived from *anti*-**187**, was found to inactive at 5 atm of hydrogen. By increasing hydrogen pressure to 45 atm, 2-methyl

tetrahydroquinoline was obtained with 84% conversion and 36% ee. The versatility of complex **198** allowed us to perform more optimization studies using this catalyst.

The reaction was found to be solvent dependant, with full conversion being observed in toluene (94%), and fairly good conversion in THF (86%) (Table 4). Methanol and dichloromethane were found to be poor solvents for this reaction. Without additive, the conversion and enantioselectivity dropped considerably. In contrast to the case with some other catalysts that are expected to operate by inner sphere mechanisms,^{90, 93b} the use of iodine as an additive afforded only trace amounts of product. On addition of 1 mol% of triphenylphosphine, the intermediate iridium hydride complexes which are responsible for catalysis were formed. The dihydride remains coordinately unsaturated in the presence of non-coordinating PF₆ anion allowing the hydride species to react with free hydrogen. The use of triphenylphosphine as an additive can be considered as an advantage over iodine since halides which may inhibit the formation of the active catalyst by competing for a coordination site. In this sense, the new chiral catalyst system seems to behave similarly to Crabtree's complex. To study the effects of other phosphines as additives, P(*o*-tol)₃ and P(2-fur)₃ were used. The use of P(*o*-tol)₃ gave good conversion (90%) but only with low ee (35%), and it required longer reaction time (18 h). When P(2-fur)₃ was used as additive, very low conversion (53%) was observed with very poor selectivity (4%). One notable feature of using P(2-fur)₃ as an additive was that the (*R*) enantiomer was formed in excess, while in all other cases, (*S*) enantiomer was the major product. This might be due to the presence of oxygen atoms participating in the transition state of enantiomer determining step by coordination.

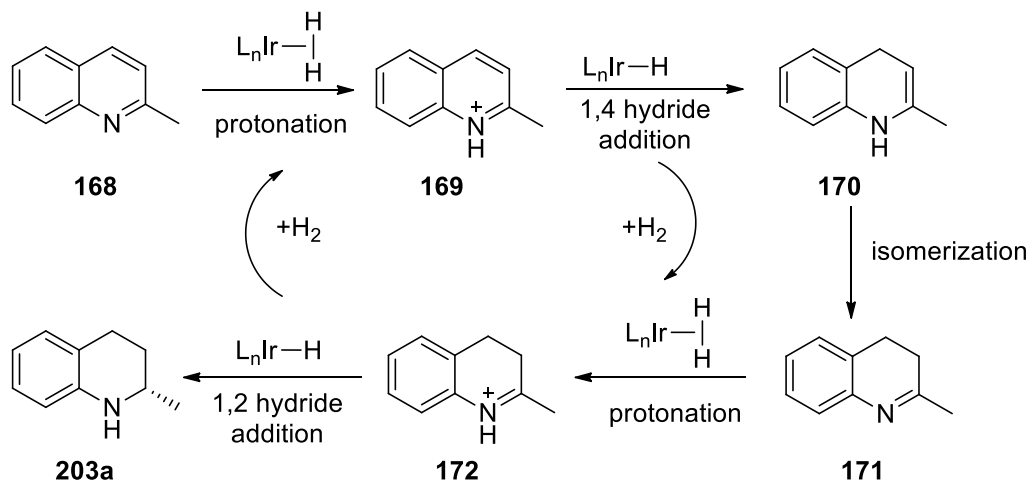


Solvent	Time	er (S:R)	Additive	Yield (%)*
PhMe	6 h	79:21	PPh ₃	94
MeOH	16 h	55:45	PPh ₃	47
CH ₂ Cl ₂	16 h	69:31	PPh ₃	71
THF	16 h	72:28	PPh ₃	86
PhMe	24 h	61:39	-	76
PhMe	24 h	-	I ₂	< 5
PhMe	18 h	67:33	P(<i>o</i> -tol) ₃	90
PhMe	18 h	48:52	P(2-fur) ₃	53

* isolated yields after column chromatography

Table 4. Optimization of the hydrogenation of 2-methyl quinoline.

Based on these observations, a proposed mechanism of the reaction considering an outer sphere mechanistic pathway, is given in Scheme 65.



Scheme 65. Proposed mechanism for the hydrogenation 2-methyl quinoline.

Assuming that similar reactive intermediates as that of Crabtree's mechanistic pathway are formed (Scheme 47); the enantioselectivity of this reaction can be explained by considering the following transition state (Figure 17). The generation of lower energy transition state formed due to CH/ π attraction between phenyl group of dihydroquinoline and the η^5 -Cp ring can give rise to lower energy TS-*si* than TS-*re*. CH/ π interaction was realized by Noyori and co-workers in rationalizing the asymmetric reduction of ketones.^{83b} Accurate explanation to mechanistic pathway and stereoselectivity requires DFT study of mechanism and origin of stereoselectivity.

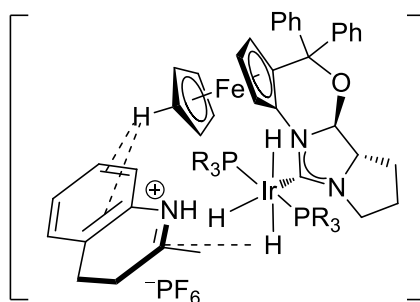
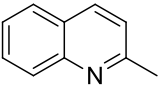
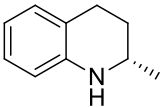
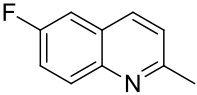
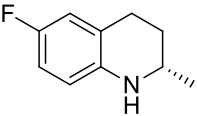
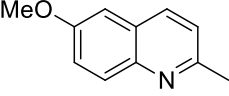
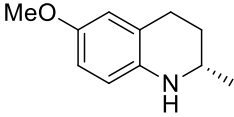
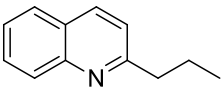
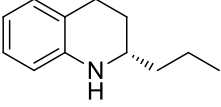
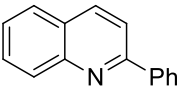
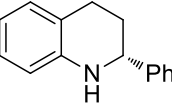


Figure 17. Proposed transition state for origin of enantioselectivity.

3.3.2. Substrate Scope for the Hydrogenation Precatalyst

After the initial catalyst screening, several substituted quinolines were subjected to hydrogenation using catalyst **198**. Among them, 2-methyl quinoline and 6-fluoro 2-methyl quinoline went to full conversion within 10 h, with **203b** giving the highest enantioselectivity of the series; 90:10 er (80% ee). (*S*)-6-Fluoro 2-methyl tetrahydroquinoline **203b** is the key intermediate in the synthesis of antibacterial agent (*S*)-flumequine **109**.⁷³ This result supports the possibility that this catalytic system

operates by outer sphere mechanism. In outer sphere mechanism, protonation at several substitutions on the quinoline are permitted, including functionalities in 2, 6- positions. The reaction selectivity was found to be sensitive to the presence of a phenyl group **203e** in 2-position. However, in all cases, the hydrogen pressure used is far lower than those typical for this type of asymmetric hydrogenation. Ketimine (*N*-(1-phenylethylidene)aniline), 2,9-dimethyl phenanthroline, 1-methyl isoquinoline and 3-methyl isoquinoline were found to be reluctant to hydrogenation under given conditions. The substrate scope for this reaction seems to be limited, depending on the pK_a of the heteroaromatic compound. By ligand modifications, the acidity of the reactive hydride species can be increased, thereby enabling protonation heteroaromatic compounds with lower pK_a s.

Substrate	Product	203	Yield (%) [*]	er (S:R)	Time
		a	94	79:21	6 h
		b	93	90:10	10 h
		c	78	79:21	24 h
		d	78	69:31	24 h
		e	25	25:75	36 h

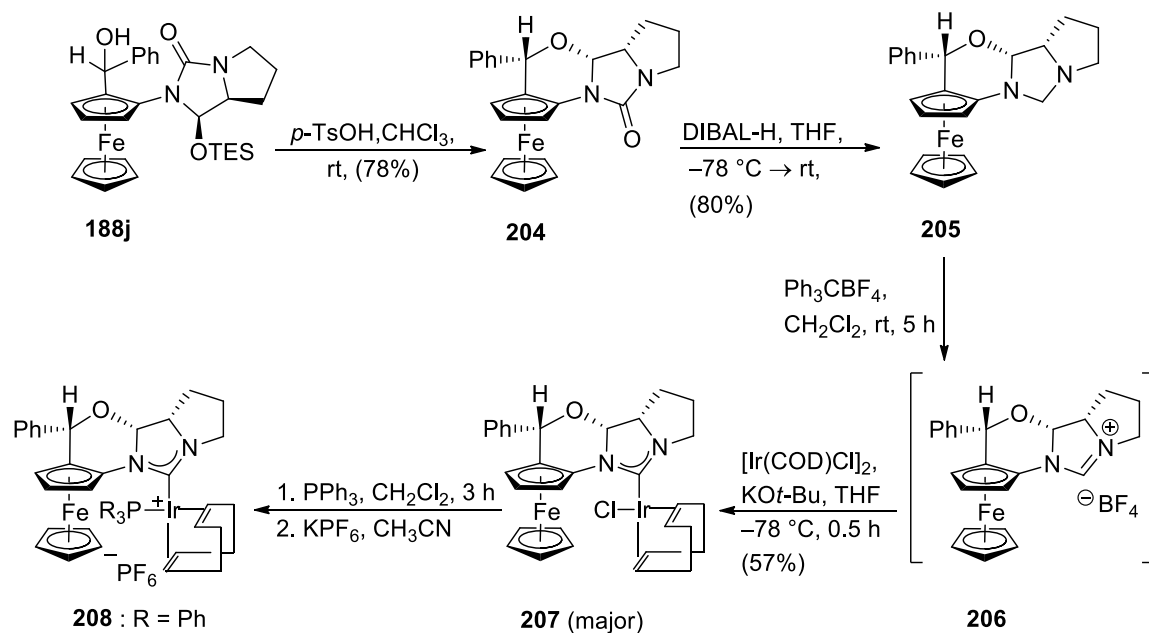
Catalytic conditions: complex **198** (1 mol %), PPh₃ (1 mol %), H₂ (5 atm), toluene, rt

^{*} isolated yields after column chromatography

Table 5. Substrate scope for the iridium catalyzed asymmetric hydrogenation.

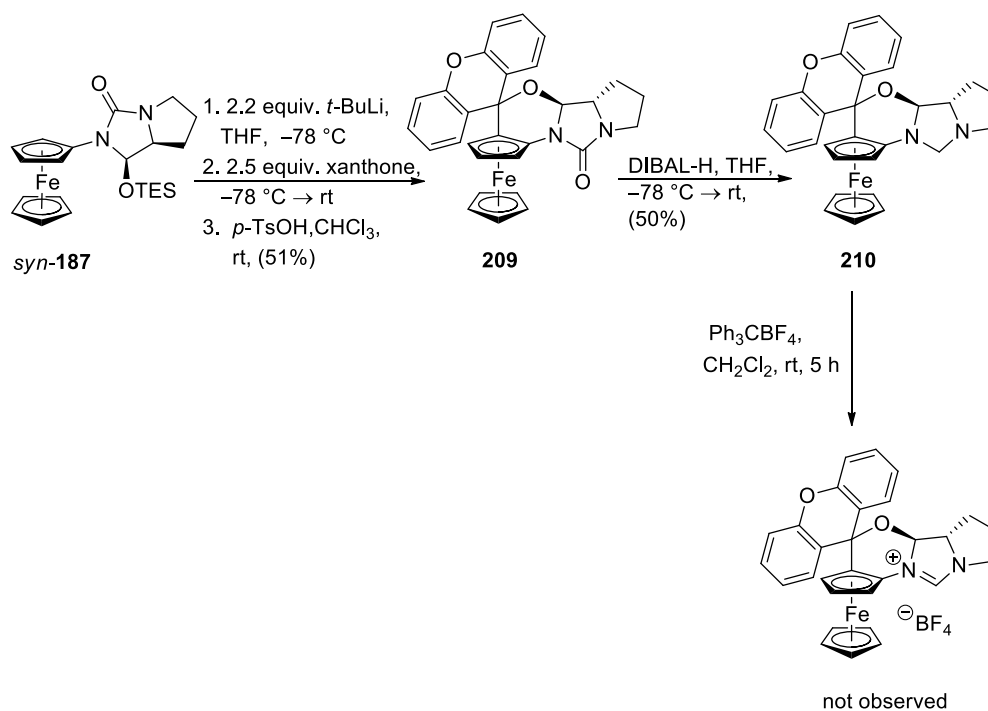
Encouraged by the results shown by catalyst **198** in asymmetric hydrogenation of quinolines where the reactivity of the catalyst **198** was similar to that exhibited by Crabtree's catalyst, our next attempt was to improve the enantioselectivity of reaction. For that, a few different catalyst systems were envisioned. Under an analogous procedure used previously to prepare **198**, complex **208** was prepared by using diastereoselective lithiation-benzaldehyde quench on *syn*-**187**. Acid mediated cyclization followed by reduction gave the amina **205** with an additional chiral center (Scheme 65). The Ir(I) complex **208** was synthesized using the same method employed for complexes **198** and **202**. The asymmetric hydrogenation of 2-methyl quinoline using complex **208** under

optimized conditions gave good conversion (88%) at low pressures (5 atm) with very low enantioselectivity (18% ee).



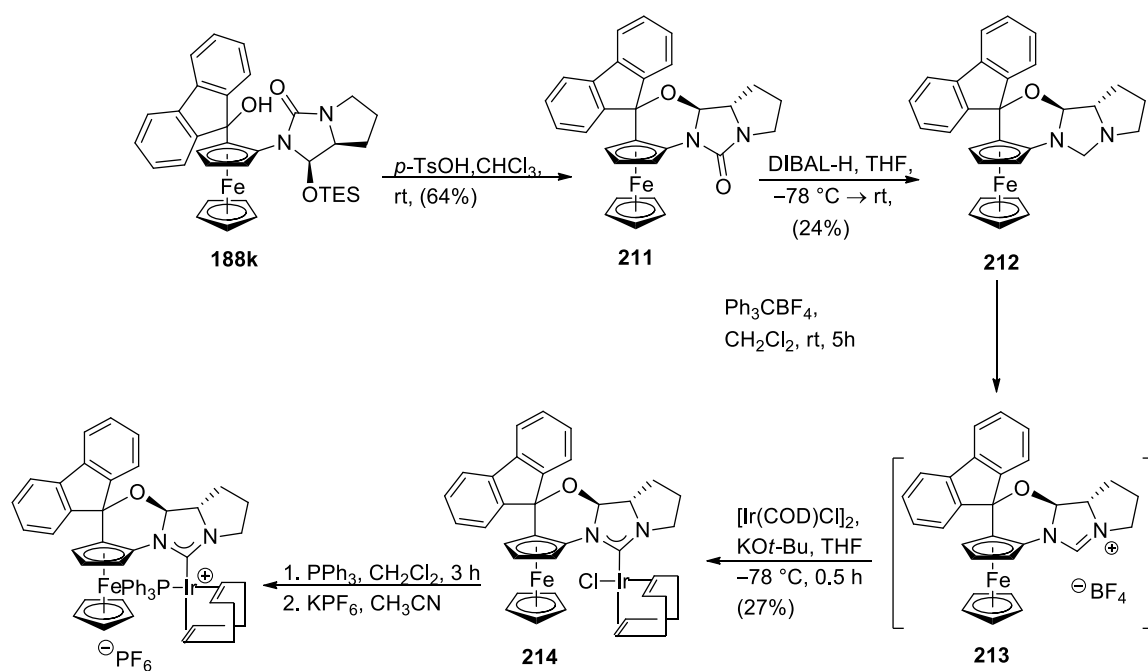
Scheme 66. Synthesis of Ir(I) complex using benzaldehyde adduct (**188j**).

Our next attempt was to make complexes where these groups are restricted to freely rotate. Using the same lithiation conditions and employing xanthone as an electrophile gave **209** after cyclization. Synthesis of compound **209** was on the assumption that this ring system may accentuate the *anti*-stereochemistry of ligand backbone because of the spirocyclic quaternary center, in addition to the steric influence. Unfortunately, the aminor **210** was found to be sensitive to oxidation and thus precluding the synthesis of an iridium complex (Scheme 66).



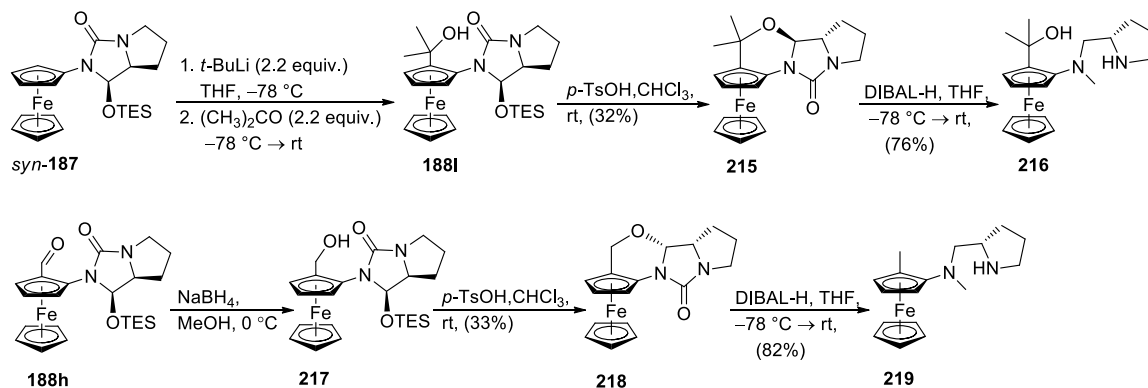
Scheme 67. Synthesis of Ir(I) complex using xanthone adduct.

Hence the reaction pathway was repeated using fluorenone as the electrophile which was taken to a neutral iridium complex (Scheme 67). Attempts to make its cationic complex were unfruitful. When asymmetric hydrogenation of 2-methyl quinoline was carried out using catalyst **214** along with 1.1 equiv. of PPh_3 under optimized conditions, no conversion was observed.



Scheme 68. Synthesis of Ir(I) complex using fluorenone adduct.

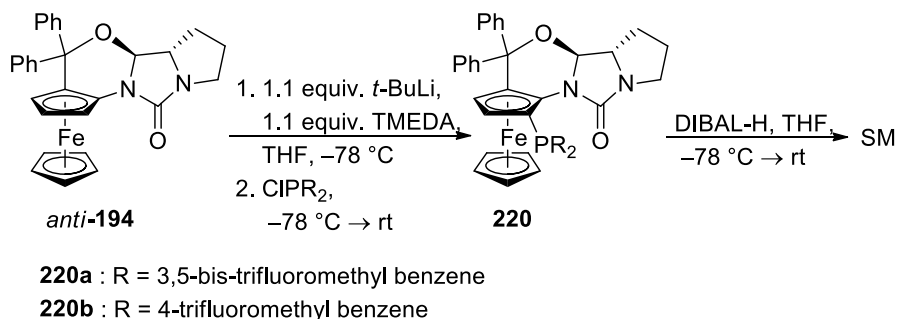
Attempts to see the effects of alkyl substituents instead of diphenyl groups on the complex were unsuccessful as well. The annulated ureas (**215**, **218**), where the former was synthesized using acetone as the electrophile and the latter by reduction of corresponding aldehyde **188h**, underwent over reduction on treatment with DIBAL-H to give **216** and **219**, respectively (Scheme 69).



Scheme 69. Attempts towards synthesis of Ir(I) complex with alkyl substituents.

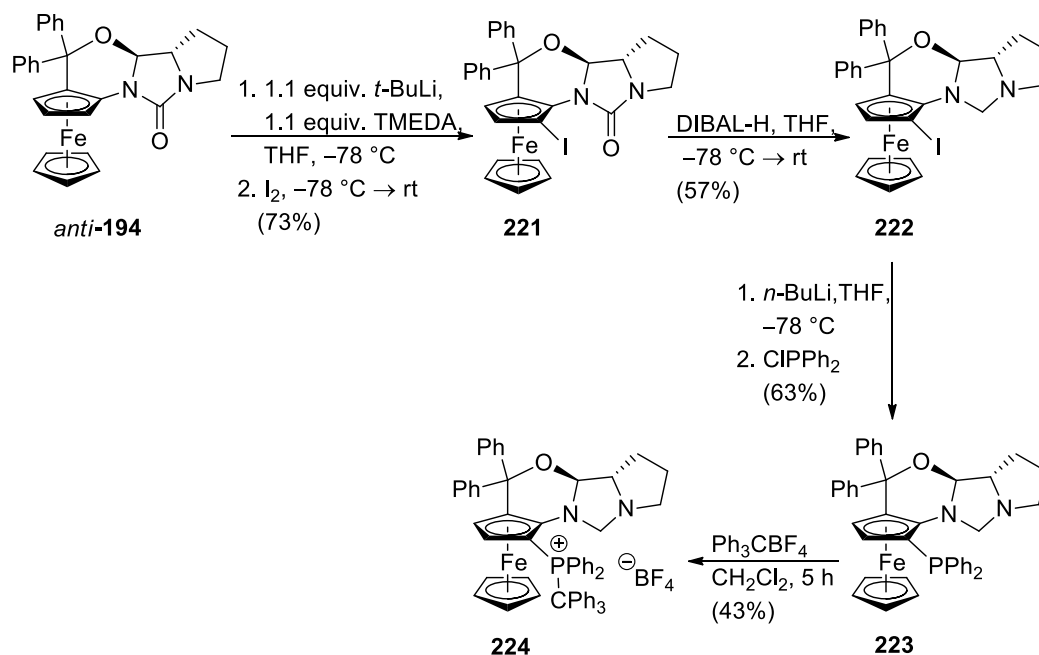
3.4. Attempts Towards Synthesis of Bidentate Ligands and Their Ir(I) Complexes

The asymmetric hydrogenation of 2-substituted quinolines using Ir(I) complex **198** gave the corresponding products in good yields with up to 80% ee. This might be attributed to the presence of metal center far from the planar chirality, thereby decreasing the extent of chiral induction. In addition to that, the use of different phosphines as additives showed changes in yield and enantioselectivity. To improve enantioselectivity, attempts were made to synthesize bidentate ligand systems with phosphine directly attached to the Cp ring. When *anti*-**194** was subjected to lithiation conditions using *t*-BuLi in presence of TMEDA, and quenched with chlorophosphines,¹²⁷ **220a** and **220b** were formed in moderate yields (Scheme 69). The phosphines with electron withdrawing groups (4-trifluoromethyl and 3,5-bis-trifluoromethyl benzene) were used as electrophiles since the use of chlorodiphenylphosphine as electrophile gave poor conversion (>20% yield), as an inseparable mixture of product and starting material. This result corroborates the expectation that urea carbonyl forms the site for base coordination for *t*-BuLi as seen from the studies on origin of stereoselectivity (Section 3.2). Subjecting these compounds to reduction using DIBAL-H at room temperature resulted in recovery of the starting material; when carried out at higher temperature, the material underwent decomposition.

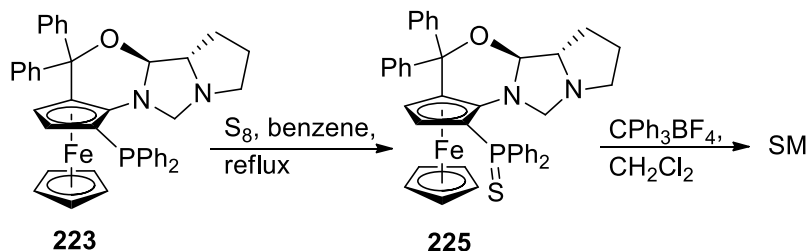


Scheme 70. Synthesis of phosphine compounds **220a,b**.

In order to avoid the possible coordination of aluminium salts to phosphine which may prevent reduction of urea **220**, the iodo compound **221** was synthesized. When the iodourea was treated with DIBAL-H, aminal **222** was obtained. Lithium-halogen exchange using *n*-BuLi, followed by quenching with chlorodiphenylphosphine gave **223** in 63% yield. Oxidation with tritylium tetrafluoroborate was unsuccessful, as the compound seemed to undergo coordination of trityl cation via phosphine **224**, which was isolated and characterized (Scheme 70). Hence, **223** was converted to the corresponding phosphine sulfide **225**, which when subjected to oxidation resulted in the recovery of starting material. The starting material was found to decompose under these conditions at elevated temperatures (Scheme 71).



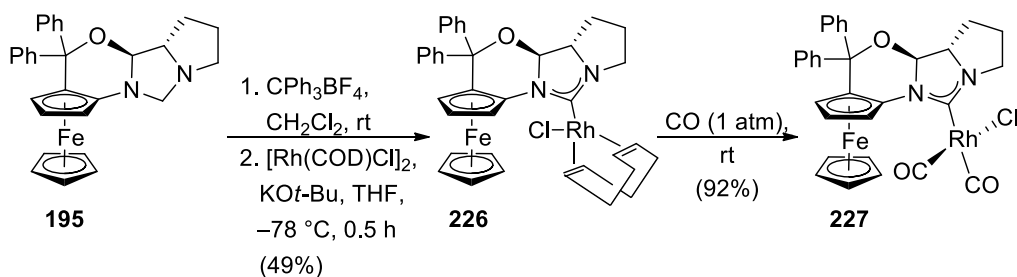
Scheme 71. Attempts towards synthesis of diphenyl phosphine containing bidentate ligands.



Scheme 72. Synthesis of phosphine sulfide **225**.

3.5. Synthesis of a Rhodium Complex Using an Annulated NHC ligand

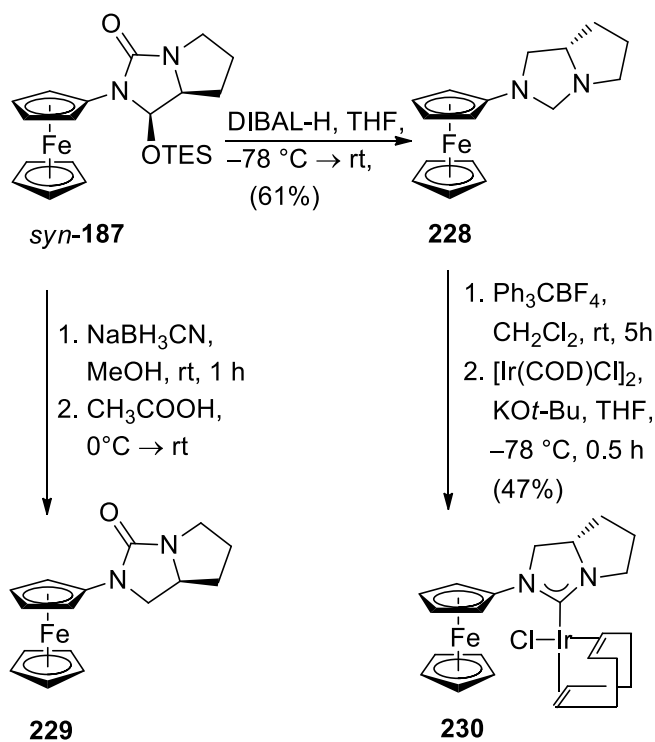
A rhodium (I) complex **226** was synthesized by following the same synthetic procedure used to prepare the Ir(I) complex **197** (Scheme 72). A simple way to evaluate the basicity of a carbene ligand is to compare the IR data of carbonyl ligands in corresponding carbene carbonyl complexes. The wavenumber of CO stretching frequency is directly proportional to the back donation from the metal center. A very basic ligand should give a relatively smaller wavenumber due to strong σ donation of the carbon atom to the metal and little π back donation from the metal center to the ligand.¹²⁸ The IR data of metal carbonyl complexes have been widely used to assess the overall donor strength of a bound carbene ligand. The stretching frequency (ν) of trans-CO moiety enables the most rigorous assessment of the electronic properties of the ligand because it is least influenced by any steric effects. To study the electron releasing capacity of the ferrocenyl substituted ligand, (NHC)RhCl(CO)₂ was synthesized and determined the stretching frequency of trans-CO ligand at $\nu = 2007 \text{ cm}^{-1}$. This is indicative of an electron-releasing capacity close to that of a dimesityl imidazol-2-ylidene (IMes) ligand (2006 cm^{-1}).¹²⁹ The use of this complex in catalytic asymmetric hydroformylation reaction is being pursued in the Metallinos group.



Scheme 73. Synthesis of rhodium complexes **226** and **227**.

3.6. Attempts Towards Non-annulated Bidentate Ligands and Their Ir(I) Complexes

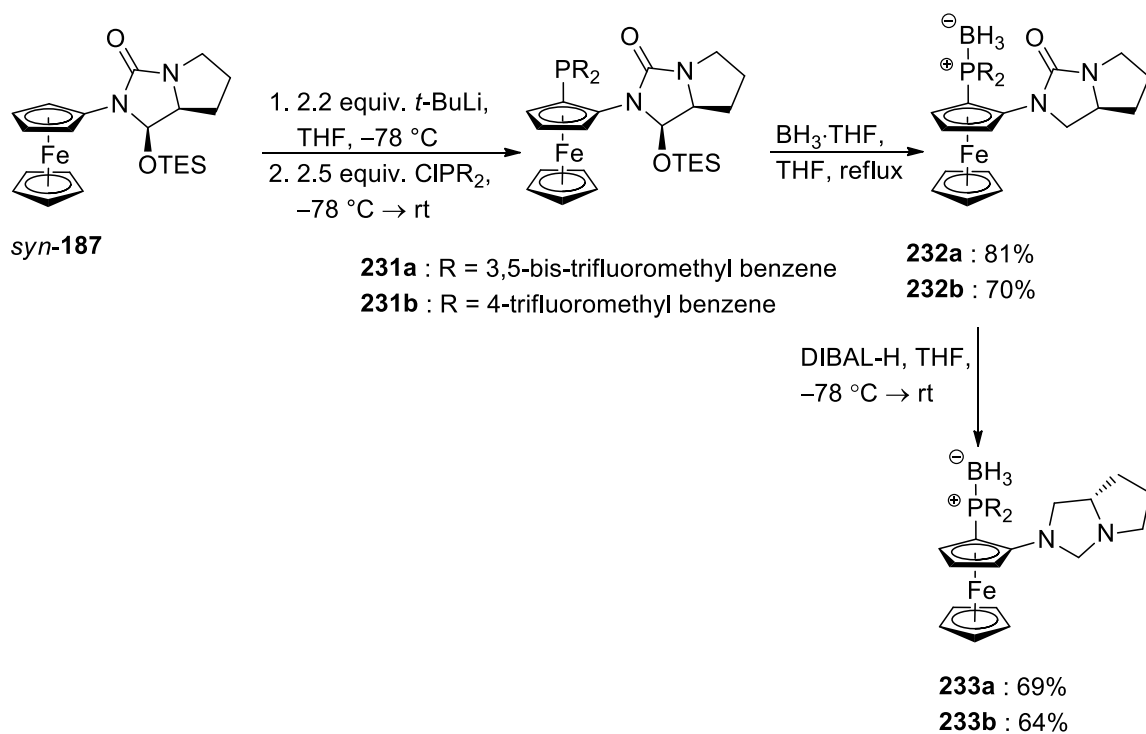
A saturated urea **229** can be synthesized from *syn*-**187** by treating with sodium cyanoborohydride and acetic acid (Scheme 73).



Scheme 74. Synthesis of neutral iridium complex **230**.

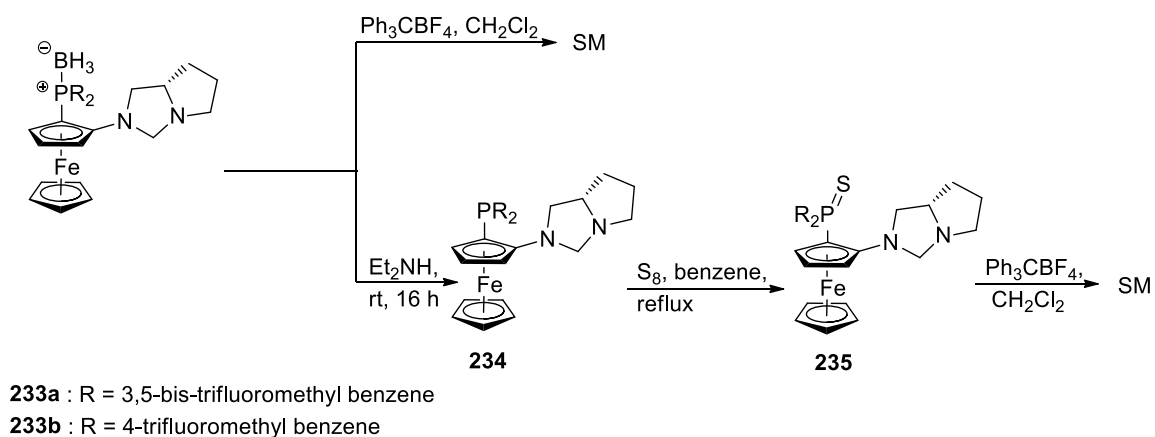
When *syn*-**187** was treated with 6 equivalents of DIBAL-H, it caused reduction of the urea moiety and removal of silyloxy group to give amina **228**. When this amina was subjected to oxidation, the imidazolinium salt was formed, which was taken to the next step as a crude mixture. Deprotonation of the imidazolinium salt followed by trapping with iridium gave the neutral iridium complex **230**. This observation encouraged us to develop a synthetic route towards the synthesis of bidentate ligands and their Ir(I) complexes.

Previous attempts to make a diphenylphosphino derivative of *syn*-**187** were unsuccessful possibly due to the presence of excess base. Previous result in the group has shown that the use of an additive, 2-dimethyl aminoethanol (DMAE) in the lithiation of BF₃-activated tertiary aminoferrocenes has shown to give high enantioselectivity.⁴⁵ To study the effect of an additive in lithiation of *syn*-**187**, different additives such as DMAE, LiCl and tetramethylethylenediamine (TMEDA) were used with 2.2 equivalents of *t*-BuLi and by using methyl iodide or tributyltin chloride as electrophiles. In all cases, the products were formed in lower yields (up to 65% for methyl substituted compound, **188d**) than the reaction done without additive.^{127d} Hence we expected that the use of chlorophosphines containing electron withdrawing groups on phenyl ring would impart stability to the resulting phosphine substituent. Thus the 3,5-bis-trifluoromethyl and 4-trifluoromethyl phosphines were prepared which on treatment with DIBAL-H were resistant to reduction. Hence the phosphine **231a** or **b** was heated to reflux with BH₃·THF which facilitated the coordination of borane to phosphine and removal of the silyloxy group to get urea **232** which then underwent reduction easily to give corresponding amina in good yields (Scheme 74).



Scheme 75. Synthesis of borane-phosphine amins.

The amins were found to be resistant to oxidation at room temperature and on heating at higher temperature, decomposition of starting material was observed (Scheme 75).



Scheme 76. Attempts towards oxidation of amination **233**.

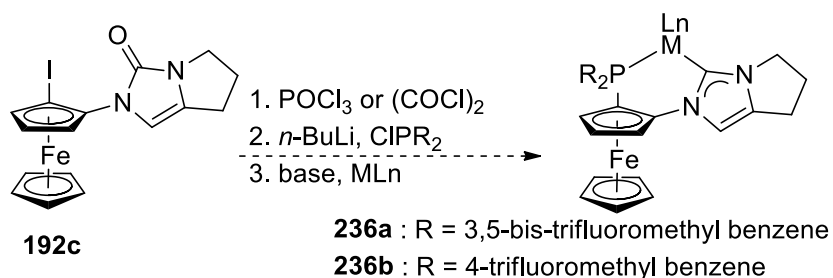
The oxidation was therefore carried out on free phosphine **234** using tritylium tetrafluoroborate which resulted in the coordination of trityl cation to phosphine (*vide supra*). Hence the phosphine was converted to phosphine sulphide **235** by heating a benzene solution of **234** with sulphur. Unfortunately, **235** was resistant to oxidation as well presumably due to the steric hindrance from sulphur.

4. Conclusions and Future Work

A feasible method for the stereoselective synthesis of planar chiral ferrocenes has been developed. The chiral auxiliary used for the synthesis was found to satisfy all the requirements of a practical chiral auxiliary. The key starting material was prepared by coupling of readily available L-proline hydantoin to iodoferrocene followed by stereoselective hydrosilylation. Upon lithiation and electrophile quench, this chiral auxiliary was found to deliver *ortho*-substituted products in >95:5 diastereoselectivity. It also provides a direct route to *ortho*-substituted planar chiral hydrolysis products by making use of a labile silyoxy moiety. The studies on the origin of stereochemistry showed that the epimeric substrate, *anti*-**187**, induced lithiation of pro- R_p rather than pro- S_p position of the ferrocene core in >95:5 dr. This reversal of stereochemistry was confirmed by X-ray analysis and by comparison solely planar chiral imidazolones derived from both *syn*- and *anti*-**187** epimers. The data were further supported by the spectroscopic studies including 1-D nOe experiments, base effects, and selective lithiation-deuteration of both epimers showing that the lithiation process is Cp ring controlled as in the case of Ugi's amine. Additional support was obtained by ground and transition state modeling of *syn*- and *anti*-**187** epimers.

Our studies towards the synthesis of advanced derivatives resulted in the preparation of an iridium complex. The cationic iridium complex prepared was used for the asymmetric hydrogenation of 2-substituted quinolines in pressures as low as 5 atm in up to 80% ee. Attempts to improve the hydrogenation stereoselectivity by synthesizing bidentate ligand systems were found to be unsuccessful. An alternative route towards the synthesis of bidentate ligand system is to make use of an *ortho*-substituted imidazolone.

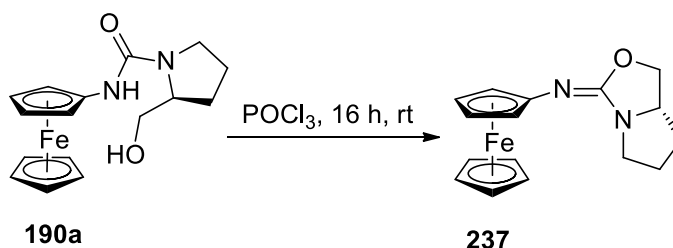
Imidazolones can be converted to imidazolyliidines, which can act as ligand precursors.⁶⁹ Thus by treating **192c** with phosphoryl oxychloride or oxalyl chloride can give corresponding chloroimidazolium salt. On treatment with base such as *t*-BuLi, carbene will be generated which can be trapped with a metal complex. The susceptibility of phosphines towards oxidation or decomposition can be ruled out by introducing the phosphino group at a later stage by metal-halogen exchange.



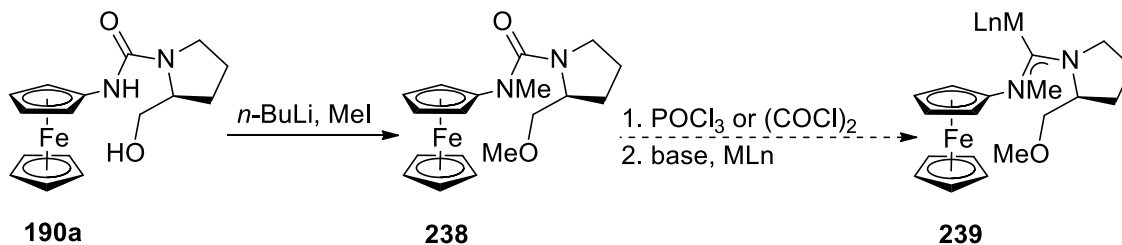
Scheme 77. Alternative route to bidentate metal complexes.

Acyclic diaminocarbenes possess some advantages over NHCs. They have donor ability in comparison with NHCs and hence displays an increased electronic density on a metal center. This property of these compounds facilitates the oxidative addition of an organic substrate to the metal center which is a key step in transition metal catalyzed organic reactions. Additionally, acyclic diaminocarbene ligands possess wider N-C-N bond angles compared to related N-heterocyclic carbenes, and, consequently, occupy more space next to a metal center. Acyclic diaminocarbenes provides greater steric control which on the one hand, increases the stability of the corresponding metal complexes and on the other hand, facilitates reductive elimination which is the final stage of cross-coupling catalytic cycle. In an attempt to make acyclic diaminocarbenes as alternative to NHCs as ligands,¹³⁰ **190a** was treated with POCl_3 at room temperature, and

underwent cyclization to give oxazol-ylidene amine **237** (Scheme 77). This can be solved by protecting the amide nitrogen and hydroxyl and then converting it to corresponding ylidene by treatment with phosphoryl oxychloride or oxalyl chloride. The carbene precursor thus generated can be treated with a base and trapped as a metal complex. By introducing a phosphino group by diastereoselective lithiation and substitution, and by using the same strategy, synthesis of bidentate metal complexes can be achieved as well.



Scheme 78. Formation of oxazol-ylidene amine **237**.




Scheme 79. Synthesis acyclic diaminocarbenes.

5. Experimental Procedures

General Experimental. All reagents were purchased from Aldrich, Fisher Scientific, Acros, Strem or Oakwood chemicals and used as received unless otherwise indicated. Tetrahydrofuran, diethyl ether and 1,4-dioxane were freshly distilled from sodium/benzophenone ketyl under an atmosphere of nitrogen. Toluene was freshly distilled from sodium under an atmosphere of nitrogen. Dichloromethane and dimethyl sulfoxide were distilled from CaH_2 under an atmosphere of nitrogen. Methanol was distilled from magnesium methoxide under argon. All alkyllithium and lithium amide bases were titrated against *N*-benzylbenzamide¹³¹ to a blue endpoint. All reactions were performed under argon in flame- or oven-dried glassware using syringe-septum cap techniques unless otherwise indicated. TLC was performed on silica gel unless otherwise stated. Column chromatography was performed on silica gel 60 (70-230 mesh). Schwartz's reagent was prepared according to a literature procedure.¹¹⁵ NMR spectra were obtained on a Bruker Avance 300, 400 or 600 MHz instrument and are referenced to the residual proton signal of the deuterated solvent for ^1H spectra, and to the carbon multiplet of the deuterated solvent for ^{13}C spectra according to published values.⁴¹ Spectroscopic data are reported as follows: (multiplicity, number of protons, coupling constant), where s = singlet, d = doublet, t = triplet, q = quartet and dd = doublet of doublets. Enantiomeric ratios were determined on an Agilent 1100 series HPLC system at $\lambda = 254$ nm on a Chiralcel OD-H column. Except for hydrogenation products, all compounds were compared against racemic material. It should be noted for HPLC measurements that response factors were not obtained for each enantiomer in all the cases and the reported enantiomeric ratios are not calibrated. FT-IR spectra were obtained on

an ATI Mattson Research Series spectrometer as KBr pellets for solids or on KBr discs for liquids and on Bruker ALPHA platinum ATR spectrometer as neat material. Optical rotations were measured on a Rudolph Research Autopol III automatic polarimeter. Mass spectra were obtained on an MSI/Kratos Concept 1S Mass Spectrometer. Combustion analyses were performed by Atlantic Microlab Inc., Norcross, GA, USA. Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Crystallographic data for the structures reported in this thesis have been deposited with the Cambridge Crystallographic Data Centre as corresponding supplementary publication number. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Iodoferrocene (22).¹³²

Following a literature procedure adapted from the synthesis of  formylferrocene;¹⁵ ferrocene (30.0 g, 0.16 mol) and potassium *t*-butoxide (2.2 g, 0.02 mol) were dissolved in 1.6 L of dry THF and the solution was cooled to $-74\text{ }^{\circ}\text{C}$ using a dry ice/acetone bath. Over a period of 35 min., *t*-BuLi (310 mL, 1.04 M in pentane, 0.32 mol) was added keeping the internal reaction temperature below $-70\text{ }^{\circ}\text{C}$. After 1 h, iodine (96.0 g, 0.38 mol) was added in one portion by increasing the flow of argon, to the reddish orange solution. The reaction mixture was then allowed to warm to $-40\text{ }^{\circ}\text{C}$ over a period of 20 min, followed by addition of water. The combined organic extract was washed with sat. aq. $\text{Na}_2\text{S}_2\text{O}_3$, water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, hexanes) afforded **22** (40 g, 0.13 mol, 80%) as an orange-brown oil which solidified on standing. mp $43\text{--}45\text{ }^{\circ}\text{C}$ [lit.¹³² mp. $44\text{--}45\text{ }^{\circ}\text{C}$]; IR (neat) ν_{max} 3091, 2919,

2852, 1405, 1377, 1337, 1104, 814 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 4.40 (t, 2H, $J = 1.5$ Hz), 4.18 (s, 5H), 4.14 (t, 2H, $J = 1.8$ Hz).

If a mixture of iodoferrocene and ferrocene was obtained, the yield of iodoferrocene was calculated as follows:

From ^1H NMR, $\text{FcI}:\text{Fc}$ was found to be 5:1 (see selected spectra).

$$\begin{aligned} M_{\text{total}} &= M_{\text{FcI}} + M_{\text{Fc}} \\ &= n_{\text{FcI}} \times \text{MW}_{\text{FcI}} + n_{\text{Fc}} \times \text{MW}_{\text{Fc}} \\ &= n_{\text{Fc}} (5 \text{MW}_{\text{FcI}} + \text{MW}_{\text{Fc}}) \end{aligned}$$

$$n_{\text{Fc}} = M_{\text{total}} / (5 \text{MW}_{\text{FcI}} + \text{MW}_{\text{Fc}})$$

$$M_{\text{total}} = 19.88 \text{ g}$$

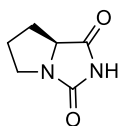
Therefore, $n_{\text{Fc}} = 0.01$ moles

$$\text{Amount of Fc present} = 0.01 \text{ moles} \times 186.04 \text{ g/mol} = 1.86 \text{ g}$$

$$\text{Amount of FcI present} = 19.88 \text{ g} - 1.86 \text{ g} = 18.02 \text{ g}.$$

$$\text{Yield} = 67\%$$

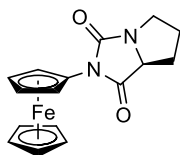
(-)-(R)-Tetrahydro-1H-pyrrolo[1,2-c]imidazole-1,3(2H)-dione (107).¹³³



According to literature procedures,¹³⁴ to a solution of L-proline **106** (50.0 g, 0.43 mol) in water (150 mL) was added potassium cyanate (43.0 g, 0.53 mol) and the reaction mixture was heated at 70 °C for 1 h to give a clear solution. The reaction mixture was allowed to cool to room temperature and 6M HCl (150 mL) was added slowly, which resulted in the evolution of gas and formation of a white precipitate. The reaction mixture was then heated to reflux for 2 h, producing a clear, slightly yellow solution. After cooling to room temperature, the reaction mixture was placed in a refrigerator for 24 h. Colorless crystals formed were filtered and washed

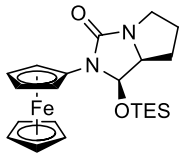
with ice-cold water to give **107** (60 g, 0.43 mol, 50%) as rod-like crystals. mp 161-162 °C (H₂O) [lit^{134d} mp 165-167 °C (H₂O)]; [α]_D¹⁸ -124 (*c* 1.0, MeOH); IR (neat) ν_{max} 3171, 3062, 2987, 2961, 2734, 1753, 1702, 1395, 1112 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.40 (bs, 1H), 4.13 (dd, 1H, *J* = 7.6, 1.6 Hz), 3.69 (dt, 1H, *J* = 15.2, 7.6 Hz), 3.21 (dq, 1H, *J* = 12.8, 4.8 Hz), 2.28-2.20 (m, 1H), 2.16-2.01 (m, 2H), 1.83-1.73 (m, 1H).

(-)-2-Ferrocenyl-7a*S*-tetrahydropyrrolo[1,2-*c*]imidazole-1,3-dione (185**).**



A mixture of iodoferrocene (6.70 g, 21.60 mmol), **107** (4.50 g, 32.40 mmol) and Cu₂O (2.50 g, 17.30 mmol) in DMSO (22 mL) were heated at 120 °C for 43 h. After cooling to room temperature, the reaction mixture was diluted with ether and washed with water (2 ×) and brine, dried over anhydrous Na₂SO₄ and the volatiles were removed under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, *R_f* = 0.22) afforded **185** (3.9 g) as an orange solid that was recrystallized from CH₂Cl₂/hexanes to give (3.7 g, 0.01 mol, 53%) orange blocks; mp 112-113 °C (CH₂Cl₂/hexanes); [α]_D²⁰ -128 (*c* 1.1, CHCl₃); CSP HPLC analysis (Chiralcel OD-H; eluent: 90:10 hexanes/*i*-PrOH, 1.0 mL/min) determined >99:1 er, >98% ee [*t_R*(minor) = 16.22 min, *t_R*(major) = 19.65 min]; IR (KBr) ν_{max} 3136, 3080, 2983, 2904, 1771, 1707, 1482, 1387, 1373 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 4.95 (s, 1H), 4.92 (s, 1H), 4.20 (s, 5H), 4.13-4.10 (m, 3H), 3.78-3.74 (m, 1H), 3.33-3.29 (m, 1H), 2.33-2.28 (m, 1H), 2.16-2.10 (m, 2H), 1.79-1.72 (m, 1H); ¹³C NMR (150.9 MHz, CDCl₃) δ 172.2, 159.2, 89.0, 69.5, 65.4, 65.3, 62.8, 62.7, 62.5, 45.9, 27.9, 26.8; EIMS [*m/z* (%)] 324 (*M*⁺, 64), 227 (100), 121 (19), 56 (26); HRMS (EI) calcd for C₁₆H₁₆N₂O₂⁵⁶Fe: 324.0561; found 324.0563. Anal. calcd for C₁₆H₁₆N₂O₂Fe: C, 59.28; H, 4.98. Found: C, 59.38; H, 5.13.

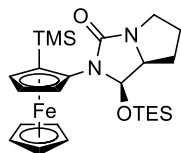
(+)-2-Ferrocenyl-1*R*-triethylsilyloxy-7a*S*-hexahydropyrrolo[1,2-*c*]imidazol-3-one
(*syn*-187**).**



Hydantoin **185** (2.00 g, 6.17 mmol) and Schwartz's reagent (2.10 g, 8.02 mmol) were suspended in THF (15 mL) and stirred at room temperature. After 10 min., the mixture became homogenous indicating consumption of starting material. At this point, solid imidazole (1.0 g, 14.2 mmol) and DMAP (68.0 mg, 0.56 mmol) were added, followed by TESCl (1.40 mL, 8.02 mmol), and the mixture was stirred at room temperature for a further 5 h. The reaction mixture was diluted diethyl ether (50 mL) and worked up with water (2 mL). The organic phase was washed with 10% CuSO₄ solution (2 × 25 mL), sat. aq. NaHCO₃ and water. The resulting precipitate was removed by filtration through a pad of Celite and the filtrate was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, *R_f* = 0.42) afforded crystalline orange solid, as a 10:1 mixture of reduction epimers. Recrystallization of this mixture from EtOH-water afforded *syn*-**187** (2.2 g, 5.0 mmol, 80%) in two crops as a diastereomerically enriched crystalline orange solid. mp 97- 98 °C (EtOH/water); [α]_D²⁰ +111 (*c* 1.0, CHCl₃); CSP HPLC analysis (Chiralcel OD-H; eluent: 97:3 hexanes/*i*-PrOH, 1.0 mL/min) determined >99:1 er, >98% ee [*t_R*(minor) = 8.73 min, *t_R*(major) = 14.37 min]; IR (KBr) ν_{max} 3083, 2953, 2910, 2876, 1693, 1501, 1411, 1085, 1006 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.44 (d, 1H, *J* = 6.3 Hz), 4.80 (s, 1H), 4.29 (s, 1H), 4.18 (s, 5H), 4.04 (s, 1H), 3.95-3.93 (m, 2H), 3.65-3.61 (m, 1H), 3.13-3.09 (m, 1H), 1.98-1.91 (m, 3H), 1.75-1.72 (m, 1H), 0.90 (t, 9H, *J* = 7.8 Hz), 0.61-0.51 (m, 6H); ¹³C NMR (150.9 MHz, CDCl₃) δ 159.2, 96.3, 82.6, 69.0, 65.1, 63.6, 62.0, 61.7, 61.5, 45.8, 26.5, 25.3, 6.8,

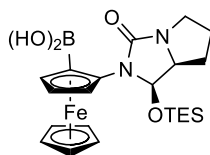
5.0; EIMS [m/z (%)] 440 (M^+ , 40), 308 (66), 243 (100), 227 (39), 103 (86), 75 (68); HRMS (EI) calcd for $C_{22}H_{32}N_2O_2Si^{56}Fe$: 440.1582; found 440.1587. Anal. calcd for $C_{22}H_{32}N_2O_2SiFe$: C, 59.99; H, 7.32. Found: C, 60.17; H, 7.59.

(+)-2-[(2*R_p*-Trimethylsilyl)ferrocenyl]-1*R*-triethylsilyloxy-7*aS*-hexahydropyrrolo[1,2-*c*]imidazol-3-one (188a) using LDA.



A solution of LDA (0.36 mL, 1.37 M in THF, 0.50 mmol) was added dropwise to a solution of *syn*-**187** (100 mg, 0.23 mmol) and TMSCl (0.07 mL, 0.57 mmol) in THF (3 mL) at $-78\text{ }^{\circ}\text{C}$ and the mixture was stirred at that temperature for 2 h. The reaction mixture was worked up by addition of water (0.5 mL) and warmed to room temperature and extracted with diethyl ether (2×10 mL). The combined organic extract was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.57$) afforded **188a** (93 mg, 0.18 mmol, 80%), as a diastereomerically enriched orange oil; $[\alpha]_D^{20} +111$ (c 1.2, $CHCl_3$); IR (KBr, neat) ν_{max} 3092, 2954, 2879, 1715, 1461, 1410, 1243 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 5.39 (d, 1H, $J = 6.3$ Hz), 4.31-4.30, (m, 1H), 4.24 (s, 5H), 4.13 (t, 1H, $J = 2.4$ Hz), 4.05-4.04 (m, 1H), 3.93-3.86 (m, 1H), 3.60-3.56 (m, 1H), 3.16-3.12 (m, 1H), 1.92-1.84 (m, 3H), 1.73-1.69 (m, 1H), 0.83 (t, 9H, $J = 7.8$ Hz), 0.48 (q, 6H, $J = 7.8$ Hz), 0.22 (s, 9H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 159.2, 98.7, 84.7, 72.1, 69.4, 69.2, 67.1, 66.8, 61.7, 46.0, 26.5, 25.3, 6.6, 4.8, 0.5; EIMS [m/z (%)] 512 (M^+ , 80), 497 (100), 482 (37), 380 (18), 365 (38), 299 (57), 103 (48), 75 (43); HRMS (EI) calcd for $C_{25}H_{40}N_2O_2Si_2^{56}Fe$: 512.1977; found 512.1972.

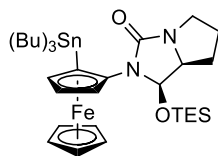
(+)-2-(Ferrocene-2*S_p*-boronic acid)-1*R*-triethylsilyloxy-7*aS*-hexahydropyrrolo[1,2-*c*]imidazol-3-one (**188b**) using LDA.



A solution of LDA (0.36 mL, 1.37 M in THF, 0.50 mmol) was added dropwise to a solution of *syn*-**187** (100 mg, 0.23 mmol) and B(Oi-Pr)₃ (0.13 mL, 0.57 mmol) in THF (3 mL) at $-78\text{ }^{\circ}\text{C}$ and the mixture was stirred at that temperature for 2 h. The reaction mixture was worked up by addition of water (0.5 mL), warmed to room temperature and extracted with diethyl ether (2×10 mL). The combined organic extract was washed with water, brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Gradient flash column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.30$, then 98:2 EtOAc/MeOH) afforded **188b** (80 mg, 0.16 mmol, 73%), as a diastereomerically enriched orange solid that was recrystallized from EtOAc/hexanes to give rod-like crystals; mp $122\text{--}124\text{ }^{\circ}\text{C}$ (EtOAc/hexanes); $[\alpha]_{\text{D}}^{20} +82$ (c 1.0, CHCl₃); X-Ray diffractometry was performed on an orange rod ($0 \times 0 \times 0\text{ mm}^3$): C₂₂H₃₃FeBN₂O₄Si: $M = 484.25\text{ g/mol}$, trigonal, $P3_2$, $a = 19.0\text{ }\text{\AA}$, $b = 19.0\text{ }\text{\AA}$, $c = 13.0\text{ }\text{\AA}$, $V = 997.6(6)\text{ }\text{\AA}^3$, $\alpha = 90^{\circ}$, $\beta = 90^{\circ}$, $\gamma = 120^{\circ}$, $Z = 8$, $D_c = \text{g/cm}^3$, $F(000) =$, $T = 298(2)\text{ K}$; X data were collected. The structure was solved by Direct Methods (SHELXTL) and refined by full-matrix least squares on F^2 resulting in final R , R_w and GOF [for X data with $F > 2\sigma(F)$] of 0.0328, 0.0646 and 1.01, respectively, for solution using the *S_p* enantiomer model [Flack parameter = 0.010(13)] [CCDC 845195 contains the crystallographic data for **188b**]; IR (KBr) ν_{max} 3354, 3097, 3083, 2956, 2877, 1650, 1468, 1399, 1377, 1331 cm^{-1} ; ¹H NMR (300 MHz, CDCl₃) δ 6.91 (s, 2H), 5.28 (d, 1H, $J = 6.6\text{ Hz}$), 4.43–4.42 (m, 1H), 4.36–4.35 (m, 1H), 4.29 (s, 5H), 4.27–4.26 (m, 1H), 4.02–3.98 (m, 1H), 3.63–3.59 (m, 1H), 3.21–3.15 (m, 1H), 2.02–1.91

(m, 3H), 1.75-1.69 (m, 1H). 0.77 (t, 9H, $J = 8.1$ Hz), 0.40-0.25 (m, 6H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 161.0, 97.7, 85.6, 72.0, 70.9, 70.0, 69.8, 68.0, 61.8, 46.0, 26.8, 24.7, 6.6, 4.5; EIMS [m/z (%)] 484 (M^+ , 12), 466 (33), 86 (65), 84 (100), 57 (46), 43 (50); HRMS (EI) calcd for $\text{C}_{22}\text{H}_{33}\text{BN}_2\text{O}_4\text{Si}^{56}\text{Fe}$: 484.1652; found 484.1631; Anal. calcd for $\text{C}_{22}\text{H}_{33}\text{N}_2\text{O}_4\text{SiFe}$: C, 54.57; H, 6.87. Found: C, 54.50; H, 6.87.

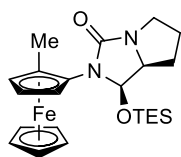
(+)-2-[(+)-2-[(*R*_p-Tributylstannyl)ferrocenyl]-1*R*-triethylsilyloxy-7*aS*-hexahydro pyrrolo[1,2-*c*]imidazol-3-one (188c) using LiTMP.



A solution of LiTMP (0.70 mL, 0.72 M in THF, 0.50 mmol) was added dropwise to a solution of *syn*-**187** (100 mg, 0.23 mmol) and Bu_3SnCl (0.15 mL, 0.57 mmol) in THF (3 mL) at -78 °C and the mixture was stirred at that temperature for 2 h. The reaction mixture was worked up by addition of water (0.5 mL), warmed to room temperature and extracted with diethyl ether (2×10 mL). The combined organic extract was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.62$) afforded **188c** (70 mg, 0.10 mmol, 45%), as a diastereomerically enriched orange oil; $[\alpha]_{\text{D}}^{20} +164$ (c 1.3, CHCl_3); IR (KBr, neat) ν_{max} 3093, 2954, 2920, 2876, 1706, 1462, 1410 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 5.40 (d, 1H, $J = 6.3$ Hz), 4.39-4.38, (m, 1H), 4.20 (s, 5H), 4.10 (t, 1H, $J = 2.4$ Hz), 3.99-3.92 (m, 2H), 3.62-3.56 (m, 1H), 3.16-3.09 (m, 1H), 2.03-1.81 (m, 3H), 1.77-1.69 (m, 1H), 1.57-1.47 (m, 6H), 1.40-1.25 (m, 6H), 1.09-0.96 (m, 6H), 0.90 (t, 9H, $J = 7.2$ Hz), 0.82 (t, 9H, $J = 7.8$ Hz), 0.46 (q, 6H, $J = 7.8$ Hz); ^{13}C NMR (75.5 MHz, CDCl_3) δ 159.2, 99.7, 83.7, 72.7, 68.9, 67.6, 66.2, 66.0, 61.7, 45.9, 29.3, 27.7, 26.8, 25.2, 13.8,

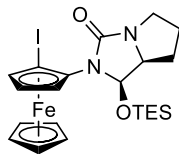
11.4, 6.7, 4.8; EIMS [$m/z(\%)$] 673 (M-C₄H₉, 96), 635 (26), 503 (29), 243 (33), 103 (100), 75 (80); HRMS (EI) calcd for C₃₀H₄₉N₂O₂Si¹²⁰Sn⁵⁶Fe: 673.1934; found 673.1944.

(+)-2-[(2*S*_p-Methyl)ferrocenyl]-1*R*-triethylsilyloxy-7*aS*-hexahydropyrrolo[1,2-*c*]imidazol-3-one (188d).



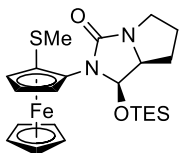
To a solution of *syn*-**187** (100 mg, 0.23 mmol) in THF (3 mL) at $-78\text{ }^{\circ}\text{C}$ was added *t*-BuLi (0.32 mL, 1.58 M in pentane, 0.51 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with MeI (0.04 mL, 0.57 mmol) and stirred for 30 min. at that temperature. Workup was conducted by addition of water (0.5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether ($2 \times 10\text{ mL}$). The combined organic extract was washed with water, brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Gradient purification by flash column chromatography (silica gel, 2:8 EtOAc/hexanes, then 3:7 EtOAc/hexanes, $R_f = 0.51$) afforded **188d** (94 mg, 0.21 mmol, 91%) as a diastereomerically enriched orange oil which solidified on standing; mp $64\text{--}65\text{ }^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{20} +133$ ($c\text{ }1.0$, CHCl₃); IR (KBr) ν_{max} 3095, 3080, 2955, 2876, 1696, 1490, 1402, 1084, 1003 cm^{-1} ; ¹H NMR (300 MHz, CDCl₃) δ 5.24 (d, 1H, $J = 6.3\text{ Hz}$), 4.20 (s, 5H), 4.06 (m, 1H), 4.01 (m, 1H), 3.94 (q, 1H, $J = 6.6\text{ Hz}$), 3.87 (t, 1H, $J = 2.7\text{ Hz}$), 3.62–3.52 (m, 1H), 3.16–3.08 (m, 1H), 1.99–1.84 (m, 3H), 1.91 (s, 3H), 1.75–1.67 (m, 1H), 0.81 (t, 9H, $J = 7.8\text{ Hz}$), 0.46–0.30 (m, 6H); ¹³C NMR (75.5 MHz, CDCl₃) δ 159.0, 93.2, 85.2, 80.6, 69.8, 67.5, 65.2, 62.9, 61.5, 46.0, 26.7, 25.2, 12.9, 6.6, 4.6; EIMS [$m/z(\%)$] 454 (M⁺, 53), 322 (86), 257 (90), 241 (50), 103 (100), 75 (78); HRMS (EI) calcd for C₂₃H₃₄N₂O₂Si⁵⁶Fe: 454.1739; found 454.1737.

(+)-2-[(2*R*_p-Iodo)ferrocenyl]-1*R*-triethylsilyloxy-7*a*S-hexahydropyrrolo[1,2-*c*]imidazol-3-one (188e).



To a solution of *syn*-**187** (100 mg, 0.23 mmol) in THF (3 mL) at -78°C was added *t*-BuLi (0.32 mL, 1.58 M in pentane, 0.51 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with a solution of $\text{ICH}_2\text{CH}_2\text{I}$ (161 mg, 0.57 mmol) in THF (3 mL) and stirred for 30 min. at that temperature. Workup was conducted by addition of water (0.5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether (2×10 mL). The combined organic extract was washed with sat. aq. $\text{Na}_2\text{S}_2\text{O}_3$, water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.44$) afforded **188e** (118 mg, 0.21 mmol, 91%) as a diastereomerically enriched orange oil; $[\alpha]_{\text{D}}^{20} +196$ (c 0.4, CHCl_3); IR (KBr) ν_{max} 3094, 2954, 2911, 2877, 1721, 1471, 1402, 1118, 1004 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3) δ 5.28 (d, 1H, $J = 6.6$ Hz), 4.45 (m, 1H), 4.37 (s, 5H), 4.22 (m, 1H), 4.15 (t, 1H, $J = 2.4$ Hz), 3.93 (q, 1H, $J = 6.6$ Hz), 3.73-3.69 (m, 1H), 3.19-3.15 (m, 1H), 2.04-1.99 (m, 2H), 1.94-1.86 (m, 1H), 1.76-1.70 (m, 1H), 0.85 (t, 9H, $J = 7.8$ Hz), 0.45-0.38 (m, 6H); ^{13}C NMR (150.9 MHz, CDCl_3) δ 158.6, 95.3, 85.0, 73.2, 72.4, 66.3, 66.2, 61.7, 46.5, 42.2, 26.4, 25.4, 6.8, 4.7; EIMS [m/z (%)] 566 (M^+ , 25), 434 (24), 308 (28), 243 (31), 103 (100), 75 (86), 43 (98); HRMS (EI) calcd for $\text{C}_{22}\text{H}_{31}\text{N}_2\text{O}_2\text{Si}^{56}\text{Fe}$: 566.0549; found 566.0544.

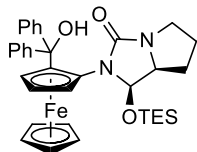
(+)-2-[(2*R_p*-Thiomethyl)ferrocenyl]-1*R*-triethylsilyloxy-7*aS*-hexahydropyrrolo[1,2-*c*]imidazol-3-one (188f**).**



To a solution of *syn*-**187** (300 mg, 0.68 mmol) in THF (7 mL) at $-78\text{ }^{\circ}\text{C}$ was added *t*-BuLi (1.06 mL, 1.41 M in pentane, 1.50 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with $(\text{MeS})_2$ (0.15 mL, 1.70 mmol) and stirred for 30 min. at that temperature. Workup was conducted by addition of water (0.5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether ($2 \times 25\text{ mL}$). The combined organic extract was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.30$) afforded **188f** (311 mg, 0.64 mmol, 94%) as a diastereomerically enriched orange glass; $[\alpha]_{\text{D}}^{20} +187$ ($c\ 1.3$, CHCl_3); IR (KBr, neat) ν_{max} 3093, 2954, 2917, 2878, 1721, 1475, 1406 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 5.41 (d, 1H, $J = 6.6\text{ Hz}$), 4.34 (m, 1H), 4.31 (s, 5H), 4.22 (m, 1H), 4.10 (t, 1H, $J = 2.4\text{ Hz}$), 3.95 (q, 1H, $J = 6.6\text{ Hz}$), 3.69-3.65 (m, 1H), 3.20-3.14 (m, 1H), 2.24 (s, 3H), 2.02-1.87 (m, 3H), 1.75-1.71 (m, 1H), 0.87 (t, 9H, $J = 8.1\text{ Hz}$), 0.54 (q, 6H, $J = 8.1\text{ Hz}$); ^{13}C NMR (75.5 MHz, CDCl_3) δ 158.9, 95.0, 84.8, 80.8, 70.6, 69.8, 65.6, 64.8, 62.0, 46.1, 26.4, 25.4, 19.8, 6.7, 4.9; EIMS [m/z (%)] 486 (M^+ , 39), 354 (78), 103 (100), 75 (77); HRMS (EI) calcd for $\text{C}_{23}\text{H}_{34}\text{N}_2\text{O}_2\text{SSi}^{56}\text{Fe}$: 486.1459; found 486.1461.

(+)-2-[2S_p-(Diphenylhydroxymethyl)ferrocenyl]-1R-triethylsilyloxy-7aS

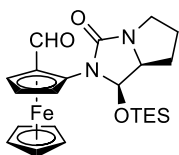
hexahydropyrrolo[1,2-c]imidazol-3-one (188g).



To a solution of *syn*-**187** (300 mg, 0.68 mmol) in THF (7 mL) at -78 °C was added *t*-BuLi (1.03 mL, 1.45 M in pentane, 1.50 mmol).

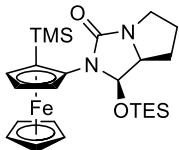
After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched a solution of Ph₂CO (311 mg, 1.70 mmol) in THF (2.5 mL) and stirred for 30 min. at that temperature. Workup was conducted by addition of water (0.5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether (2 × 25 mL). The combined organic extract was washed with water, brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 2:8 EtOAc/hexanes, R_f = 0.40) afforded **188g** (369 mg, 0.59 mmol, 87%) as a diastereomerically enriched orange solid; mp 65-66 °C; $[\alpha]_D^{20}$ +137 (c 0.7, CHCl₃); IR (KBr) ν_{\max} 3247, 3087, 3058, 2957, 2878, 1682, 1469, 1410 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 8.14 (s, 1H), 7.54-7.51 (m, 2H), 7.33-7.09 (m, 8H), 5.49 (d, 1H, J = 7.2 Hz), 4.45 (s, 5H), 4.27 (m, 1H), 3.94 (t, 1H, J = 2.7 Hz), 3.52-3.41 (m, 2H), 3.38 (m, 1H), 2.98-2.89 (m, 1H), 1.62-1.33 (m, 3H), 1.29-1.22 (m, 1H), 0.92 (t, 9H, J = 7.8 Hz), 0.61 (q, 6H, J = 7.8 Hz); ¹³C NMR (75.5 MHz, CDCl₃) δ 160.7, 147.1, 146.1, 128.1, 127.3, 127.2, 127.0, 126.3, 126.0, 92.0, 90.2, 81.6, 75.7, 72.0, 70.0, 65.9, 62.5, 62.2, 47.3, 24.0, 23.9, 6.8, 4.7; EIMS [m/z (%)] 622 (M^+ , 1), 490 (57), 103 (61), 84 (100), 43 (55); HRMS (EI) calcd for C₃₅H₄₂N₂O₃Si⁵⁶Fe: 622.2314; found 622.2308. Anal. calcd for C₃₅H₄₂N₂O₃SiFe: C, 67.51; H, 6.80. Found: C, 67.61; H, 6.81.

(+)-2-[(2*S_p*-Formyl)ferrocenyl]-1*R*-triethylsilyloxy-7*aS*-hexahydropyrrolo[1,2-*c*]imidazol-3-one) (188h).



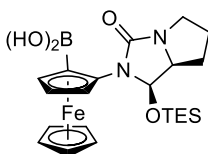
To a solution of *syn*-**187** (100 mg, 0.23 mmol) in THF (3 mL) at $-78\text{ }^{\circ}\text{C}$ was added *t*-BuLi (0.35 mL, 1.45 M in pentane, 0.51 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with DMF (0.04 mL, 0.57 mmol) and stirred for 30 min. at that temperature. Workup was conducted by addition of water (0.5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether ($2 \times 10\text{ mL}$). The combined organic extract was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.27$) afforded the major diastereomer, **S_p-188h** (74 mg, 0.16 mmol, 70%), just after the minor diastereomer, **R_p-188h** (4 mg, 0.01 mmol, 4%); Data for **S_p-188h**, a red-orange oil, are as follows: $[\alpha]_{\text{D}}^{20} +720$ ($c\ 0.2$, CHCl_3); IR (KBr, neat) ν_{max} 3097, 2956, 2913, 2878, 1710, 1671, 1472, 1442, 1401 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 10.09 (s, 1H), 5.26 (d, 1H, $J = 6.3\text{ Hz}$), 4.80-4.79 (m, 1H), 4.53-4.52 (m, 1H), 4.46-4.44 (m, 1H), 4.38 (s, 5H), 3.94 (q, 1H, 6.6 Hz), 3.63-3.55 (m, 1H), 3.18-3.10 (m, 1H), 1.99-1.86 (m, 3H), 1.75-1.71 (m, 1H), 0.77 (t, 9H, $J = 7.8\text{ Hz}$), 0.45-0.28 (m, 6H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 195.6, 159.1, 96.2, 84.7, 73.9, 71.2, 70.3, 68.6, 65.0, 61.7, 45.9, 26.4, 25.0, 6.6, 4.5; EIMS [m/z (%)] 468 (M^+ , 14), 336 (31), 243 (40), 103 (97), 75 (100), 57 (65), 43 (81); HRMS (EI) calcd for $\text{C}_{23}\text{H}_{32}\text{N}_2\text{O}_3\text{Si}^{56}\text{Fe}$: 468.1531; found 468.1533.

(+)-2-[(2*R*_p-Trimethylsilyl)ferrocenyl]-1*R*-triethylsilyloxy-7*aS*-hexahydropyrrolo[1,2-*c*]imidazol-3-one (188a) using *t*-BuLi.



To a solution of *syn*-**187** (100 mg, 0.23 mmol) in THF (3 mL) at $-78\text{ }^{\circ}\text{C}$ was added *t*-BuLi (0.32 mL, 1.58 M in pentane, 0.51 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with TMSCl (0.07 mL, 0.57 mmol) and stirred for 30 min. at that temperature. Workup was conducted by addition of water (0.5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether ($2 \times 10\text{ mL}$). The combined organic extract was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.57$) afforded **188a** (98 mg, 0.19 mmol, 84%) as a diastereomerically enriched orange oil; $[\alpha]_{\text{D}}^{20} +109$ ($c\ 1.7$, CHCl_3). All spectroscopic data matched LDA-derived **188a** above.

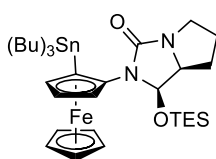
(+)-2-(Ferrocene-2*S*_pboronicacid)-1*R*-triethylsilyloxy-7*aS*-hexahydropyrrolo[1,2-*c*]imidazol-3-one (188b) using *t*-BuLi.



To a solution of *syn*-**187** (100 mg, 0.23 mmol) in THF (3 mL) at $-78\text{ }^{\circ}\text{C}$ was added *t*-BuLi (0.42 mL, 1.20 M in pentane, 0.51 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with $\text{B}(\text{OEt})_3$ (0.01 mL, 0.57 mmol) and stirred for 30 min. at that temperature. Workup was conducted by addition of water (0.5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether ($2 \times 10\text{ mL}$). The combined organic extract was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash

column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.30$, then 98:2 EtOAc/MeOH) afforded **188b** (89 mg, 0.18 mmol, 80%), as a diastereomerically enriched orange solid that was recrystallized from EtOAc/hexanes to give rod like crystals; mp 122-124 °C (EtOAc/hexanes); $[\alpha]_D^{20} +80$ (c 1.0, CHCl_3). All spectroscopic data and mp matched LDA-derived **188b** above.

(+)-2-[(*R*_p-Tributylstannyl)ferrocenyl]-1*R*-triethylsilyloxy-7*aS*-hexahydropyrrolo [1,2-*c*]imidazol-3-one (188c**) using *t*-BuLi.**



To a solution of *syn*-**187** (80.0 mg, 0.18 mmol) in THF (2 mL) at -78 °C was added *t*-BuLi (0.31 mL, 1.30 M in pentane, 0.40 mmol). After stirring for 30 min, a distinct colour change from orange to orange-red was observed. The solution was quenched with Bu_3SnCl (0.12 mL, 0.45 mmol) and stirred for 30 min. at that temperature. Workup was conducted by addition of water (0.5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether (2×10 mL). The combined organic extract was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.62$) afforded **188c** (116 mg, 0.17 mmol, 87%) as a diastereomerically enriched orange oil; $[\alpha]_D^{20} +170$ (c 0.8, CHCl_3); All spectroscopic data matched LiTMP-derived **188c** above.

Transmetalation of stannane 188c to make methyl adduct 188d.

A solution of **188c** (60.0 mg, 0.08 mmol) in THF (2 mL) was cooled to -78 °C, treated with *n*-BuLi (0.04 mL, 2.39 M in hexanes, 0.089 mmol) and stirred for 30 min. The solution was quenched with MeI (7.0 μL , 0.12 mmol) and stirred for another 30 min. at that temperature. Workup was conducted by addition of water (1 mL) and, after warming

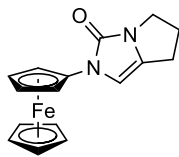
to room temperature, the reaction mixture was extracted with Et₂O (3 × 10 mL). The combined organic phase was washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. Flash column chromatography (silica gel, 3:7 EtOAc/hexanes, *R_f* = 0.51) afforded **188d** (31 mg, 0.07 mmol, 86%) as a diastereomerically enriched orange oil which solidifies on standing; mp 64-65 °C; [α]_D²⁰ +135 (*c* 0.8, CHCl₃). Spectroscopic data matched that reported for *t*-BuLi derived **188d** above.

Transmetalation of stannane **188c** to make boronic acid **188b**.

A solution of **188c** (38.0 mg, 0.05 mmol) in THF (1 mL) was cooled to -78 °C, treated with *n*-BuLi (0.02 mL, 2.39 M in hexanes, 0.06 mmol) and stirred for 30 min. The solution was quenched with B(OEt)₃ (13.0 μ L, 0.08 mmol) and stirred for another 30 min. at that temperature. Workup was conducted by addition of water (5 mL) and, after warming to room temperature, the reaction mixture was extracted with Et₂O (3 × 10 mL). The combined organic phase was washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, 3:7 EtOAc/hexanes, *R_f* = 0.30) to give **188b** (23 mg, 0.05 mmol, 92%) as a diastereomerically enriched orange solid that was recrystallized from EtOAc/hexanes to give rod like crystals; mp 124-126 °C; [α]_D²⁰ +79 (*c* 1.13, CHCl₃). Spectroscopic data and mp matched that reported for LDA or *t*-BuLi derived **188b** above.

Ferrocenyl-2,5,6,7-tetrahydropyrrolo[1,2-*c*]imidazol-3-one (**192a**).

A solution of *syn*-**187** (140 mg, 0.43 mmol) and *p*-toluenesulfonic acid monohydrate (326 mg, 1.72 mmol) in CHCl₃ (5 mL) was heated to reflux for 30 min.. The solution was

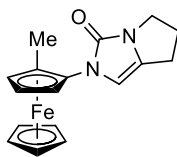


cooled to room temperature, diluted with chloroform (20 mL) and was washed sequentially with sat. aq. NaHCO_3 , H_2O , brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure.

Purification by flash column chromatography (silica gel, EtOAc, $R_f = 0.20$) afforded **192a** (124 mg, 0.40 mmol, 94%) as orange solid; mp 193-194 °C; IR (KBr) ν_{max} 3095, 2991, 2961, 2922, 1678, 1638, 1507, 1413 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 6.13 (s, 1H), 4.68 (t, 2H, $J = 1.5$ Hz), 4.18 (s, 5H), 4.05 (t, 2H, $J = 1.5$ Hz), 3.71 (t, 2H, $J = 6.9$ Hz), 2.73 (t, 2H, $J = 6.6$ Hz), 2.46-2.39 (m, 2H, $J = 7.2$ Hz); ^{13}C NMR (75.5 MHz, CDCl_3) δ 149.1, 127.0, 101.7, 95.1, 69.1, 64.9, 61.0, 42.2, 27.9, 22.8; EIMS [m/z (%)] 308 (M^+ , 100), 243 (53), 73 (21); HRMS (EI) calcd for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}^{56}\text{Fe}$: 308.0612; found 308.0579.

(–)-2-[(2*S_p*-Methyl)ferrocenyl]-2,5,6,7-tetrahydropyrrolo[1,2-c]imidazol-3-one

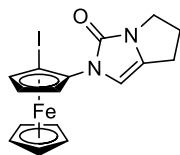
(192b).



A solution of **188d** (100 mg, 0.22 mmol) and *p*-toluenesulfonic acid monohydrate (168 mg, 0.88 mmol) in CHCl_3 (2 mL) was heated to reflux for 30 min.. The solution was cooled to room temperature, diluted with chloroform (10 mL) and was washed sequentially with sat. aq. NaHCO_3 , H_2O , brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, EtOAc, $R_f = 0.32$) afforded **192b** (65 mg, 0.20 mmol, 91%) as orange solid; mp 137-138 °C; $[\alpha]_{\text{D}}^{20} -29$ (c 1.0, CHCl_3); CSP HPLC analysis (Chiralcel OD-H; eluent: 50:50 hexanes/*i*-PrOH, 1.0 mL/min) determined 100:1 er, 98% ee [$t_{\text{R}}(\text{minor}) = 6.21$ min, $t_{\text{R}}(\text{major}) = 8.35$ min]; IR (KBr) ν_{max} 3123, 3087, 2961, 2921, 1682, 1637, 1493, 1410 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 6.31 (s, 1H), 4.33 (m, 1H), 4.16 (s, 5H), 4.06 (m, 1H), 3.98 (t, 1H, $J = 2.4$ Hz), 3.70 (t, 2H, $J = 6.9$ Hz), 2.74 (t,

2H, $J = 6.9$ Hz), 2.40 (quin, 2H, $J = 6.9$ Hz), 2.04 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 150.0, 125.8, 104.9, 93.8, 79.8, 69.6, 67.3, 64.3, 63.8, 42.2, 27.9, 22.8, 13.3; EIMS [m/z (%)] 322 (M^+ , 100), 257 (89), 84 (50); HRMS (EI) calcd for $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}^{56}\text{Fe}$: 322.0768; found 322.0760.

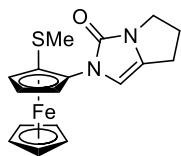
(-)-2-[2*R_p*-(Iodo)ferrocenyl]-2,5,6,7-tetrahydropyrrolo[1,2-*c*]imidazol-3-one (192c).



A solution of **188e** (98.0 mg, 0.17 mmol) and *p*-toluene sulfonic acid monohydrate (131 mg, 0.69 mmol) in CHCl_3 (5 mL), heated to reflux for 30 min.. The solution was cooled to room temperature, diluted with chloroform (10 mL) and was washed sequentially with sat. aq. NaHCO_3 , water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, EtOAc, $R_f = 0.23$) afforded **192c** (67 mg, 0.15 mmol, 90%) as orange glass; $[\alpha]_{\text{D}}^{20} -59$ (c 0.8, CHCl_3); IR (KBr, neat) ν_{max} 3153, 3093, 2958, 2927, 1690, 1638, 1487, 1409 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 6.55 (s, 1H), 4.78 (m, 1H), 4.40 (m, 1H), 4.25 (s, 5H), 4.24 (m, 1H), 3.72 (t, 2H, $J = 6.9$ Hz), 2.78 (t, 2H, $J = 6.9$ Hz), 2.42 (quin, 2H, $J = 6.9$ Hz); ^{13}C NMR (75.5 MHz, CDCl_3) δ 150.1, 125.7, 104.8, 95.2, 72.6, 72.0, 67.1, 66.4, 42.3, 37.1, 27.9, 22.8; EIMS [m/z (%)] 434 (M^+ , 57), 308 (39), 243 (40), 84 (100); HRMS (EI) calcd for $\text{C}_{16}\text{H}_{15}\text{N}_2\text{OI}^{56}\text{Fe}$: 433.9578; found 433.9571.

(-)-2-[2*R_p*-(Thiomethyl)ferrocenyl]-2,5,6,7-tetrahydropyrrolo[1,2-*c*]imidazol-3-one (192d).

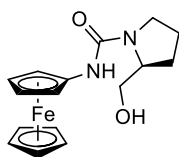
A solution of **188f** (237 mg, 0.49 mmol) and *p*-toluenesulfonic acid monohydrate (371 mg, 1.95 mmol) in CHCl_3 (5 mL), heated to reflux for 30 min.. The solution was cooled



to room temperature, diluted with chloroform (10 mL), and was washed sequentially with sat. aq. NaHCO₃, H₂O, brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure.

Purification by flash column chromatography (silica gel, EtOAc, R_f = 0.20) afforded **188d** (163 mg, 0.46 mmol, 93%) as orange glass; $[\alpha]_D^{20}$ -98 (c 1.4, CHCl₃); IR (KBr, neat) ν_{\max} 3152, 3092, 2976, 2918, 1682, 1636, 1486, 1408 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.76 (s, 1H), 4.91 (m, 1H), 4.27 (m, 1H), 4.24 (s, 5H), 4.19 (t, 1H, J = 2.7 Hz), 3.72 (t, 2H, J = 7.2 Hz), 2.78 (t, 2H, J = 7.2 Hz), 2.43 (quin, 2H, J = 7.2 Hz), 2.16 (s, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 150.2, 125.7, 104.7, 95.6, 74.9, 70.5, 70.4, 67.4, 65.6, 42.3, 27.9, 22.9, 20.5; EIMS [m/z (%)] 354 (M^+ , 100), 339 (17), 289 (18), 274 (29); HRMS (EI) calcd for C₁₇H₁₈N₂OS⁵⁶Fe: 354.0489; found 354.0492.

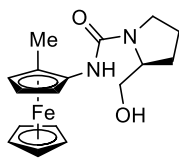
(-)-2*S*-Hydroxymethylpyrrolidine-1-carbox-(ferrocenyl)-amide (191a).



A mixture of *syn*-**187** (100 mg, 0.23 mmol) and K₂CO₃ (190 mg, 1.38 mmol) in MeOH (4 mL) was heated to reflux for 30 min.. After cooling to room temperature, the mixture was passed through Celite, rinsed well with CH₂Cl₂ and concentrated under reduced pressure. The crude hemiaminal was redissolved in abs. EtOH (5 mL), treated with NaBH₄ (52.0 mg, 1.38 mmol) and heated to reflux for another 30 min.. After cooling to 0 °C, workup was performed by careful addition of sat. aq. NH₄Cl (2 mL). The excess EtOH was evaporated under reduced pressure and the mixture was extracted with CH₂Cl₂ (2 × 20 mL), washed with H₂O, brine, dried over anhydrous Na₂SO₄ and was concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 96:4 EtOAc/Et₃N, R_f = 0.20) afforded **191a** (70 mg, 0.18 mmol, 93%) as orange solid; mp 208-210 °C

(EtOAc/hexanes); $[\alpha]_D^{18} -3$ (c 1.0, CHCl_3); IR (KBr) ν_{max} 3364, 3299, 3093, 2953, 2925, 2872, 1716, 1641, 1552, 1492, 1457 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3 , rotameric) δ 5.04 (b, 1H), 4.51 (b, 1H), 4.43 (b, 1H), 4.13 (s, 5H), 3.94 (m, 3 H), 3.63-3.60 (m, 1H), 3.54-3.47 (m, 2H), 3.31-3.30 (m, 1H), 2.03-1.93 (m, 1H), 1.86-1.80 (m, 2H), 1.58-1.52 (m, 1H); ^{13}C NMR (75.5 MHz, CDCl_3 , rotameric) δ 157.1, 98.2, 69.3, 67.4, 64.6, 64.5, 61.5, 60.2, 53.5, 47.1, 47.0, 28.7, 23.9; EIMS [m/z (%)] 400 (M^+ , 12), 300 (23), 299 (100), 121 (23), 70 (47); HRMS (EI) calcd for $\text{C}_{19}\text{H}_{28}\text{N}_2\text{O}_2\text{Si}^{56}\text{Fe}$: 400.1269; found 400.1263.

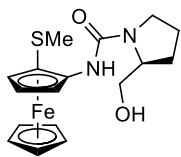
(-)-2S-Hydroxymethylpyrrolidine-1-carbox-[2S_p-(methyl)ferrocenyl]-amide (191b**).**



A mixture of **188d** (200 mg, 0.44 mmol) and K_2CO_3 (365 mg, 2.64 mmol) in MeOH (5 mL) was heated to reflux for 30 min.. After cooling to room temperature, the mixture was passed through Celite, rinsed well with CH_2Cl_2 and concentrated under reduced pressure. The crude hemiaminal was redissolved in abs. EtOH (5 mL), treated with NaBH_4 (100 mg, 2.64 mmol), and heated to reflux for another 30 min.. After cooling to 0 °C, workup was performed by careful addition of sat. aq. NH_4Cl (5 mL). The excess EtOH was evaporated under reduced pressure and the mixture was extracted with CH_2Cl_2 (2×20 mL), washed with H_2O , brine, dried over anhydrous Na_2SO_4 and was concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 96:4 EtOAc/ Et_3N , $R_f = 0.33$) afforded **191b** (137 mg, 0.40 mmol, 91%) as an orange solid; mp 139-140 °C; $[\alpha]_D^{20} -181$ (c 1.59, CHCl_3); IR (KBr) ν_{max} 3340, 3094, 3008, 2974, 2931, 2875, 1638, 1537, 1455 cm^{-1} ; ^1H NMR (600 MHz, CD_3OD) δ 4.38 (s, 1H), 4.08 (s, 5H), 4.02-3.98 (m, 1H), 3.97 (s, 1H), 3.88 (s, 1H), 3.72 (dd, 1H, $J = 10.8, 1.5$ Hz), 3.67-3.59 (m, 2H), 3.39-3.34 (m, 1H), 2.16-2.09 (m, 1H), 1.99 (s, 3H), 1.93-1.85 (m, 2H), 1.78-1.74 (m, 1H); ^{13}C

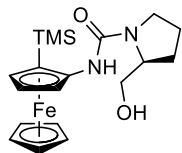
NMR (150.9 MHz, CD₃OD) δ 158.8, 93.5, 78.2, 69.2, 66.0, 65.8, 64.7, 62.5, 60.2, 46.9, 28.6, 23.3, 11.4; EIMS [m/z(%)] 342 (M⁺, 11), 241 (100); HRMS (EI) calcd for C₁₇H₂₂N₂O₂⁵⁶Fe: 342.1030; found 342.1030.

(-)-2S-Hydroxymethylpyrrolidine-1-carbox-[2R_p-(thiomethyl)ferrocenyl]-amide (191c).



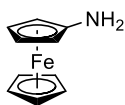
A mixture of **188f** (232 mg, 0.48 mmol) and K₂CO₃ (396 mg, 2.86 mmol) in MeOH (6 mL) was heated to reflux for 30 min.. After cooling to room temperature, the mixture was passed through Celite, rinsed well with CH₂Cl₂ and concentrated under reduced pressure. The crude hemiaminal was redissolved in abs. EtOH (6 mL), treated with NaBH₄ (108 mg, 2.86 mmol), and heated to reflux for another 30 min.. After cooling to 0 °C, workup was performed by careful addition of sat. aq. NH₄Cl (5 mL). The excess EtOH was evaporated under reduced pressure and the mixture was extracted with CH₂Cl₂ (2 × 20 mL), washed with H₂O, brine, dried over anhydrous Na₂SO₄ and was concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 96:4 EtOAc/Et₃N, R_f = 0.33) afforded **191c** (164 mg, 0.44 mmol, 92%) as an orange glass; [α]_D²⁰ -344 (c 1.4, CHCl₃); IR (KBr) ν_{max} 3351, 3092, 3008, 2954, 2920, 2873, 1628, 1542, 1492, 1429 cm⁻¹; ¹H NMR (300 MHz, CDCl₃, rotameric) δ 5.12 (b, 0.5 H), 5.07 (b, 0.5H), 4.18 (b, 2H), 4.11 (s, 5H), 4.05 (t, 1H, J = 2.4 Hz), 3.71-3.44 (m, 5H), 2.15 (s, 1.5H), 2.14 (s, 1.5H), 2.09-1.94 (m, 3H), 1.68-1.64 (m, 1H); ¹³C NMR (75.5 MHz, CDCl₃, rotameric) δ 156.5, 156.2, 98.8, 71.0, 70.2, 68.7, 67.5, 64.5, 62.0, 60.6, 47.0, 28.6, 28.5, 24.21, 24.17, 20.85, 20.79; EIMS [m/z(%)] 374 (M⁺, 7), 273 (95), 230 (35), 84 (100), 70 (37); HRMS (EI) calcd for C₁₇H₂₂N₂O₂S⁵⁶Fe: 374.0751; found 374.0749.

(-)-2*S*-Hydroxymethylpyrrolidine-1-carbox-[2*R_p*-(trimethylsilyl)ferrocenyl]-amide (191d).



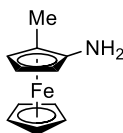
A mixture of **188a** (237 mg, 0.46 mmol) and K₂CO₃ (384 mg, 2.77 mmol) in MeOH (5 mL), heated to reflux for 30 min.. After cooling to room temperature, the mixture was passed through Celite, rinsed well with CH₂Cl₂ and concentrated under reduced pressure. The crude hemiaminal was redissolved in abs. EtOH (5 mL), treated with NaBH₄ (105 mg, 2.77 mmol) and heated to reflux for another 30 min.. After cooling to 0 °C, workup was performed by careful addition of sat. aq. NH₄Cl (5 mL). The excess EtOH was evaporated under reduced pressure and the mixture was extracted with CH₂Cl₂ (2 × 20 mL), washed with H₂O, brine, dried over anhydrous Na₂SO₄ and was concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 96:4 EtOAc/Et₃N, *R_f* = 0.57) afforded **191d** (164 mg, 0.41 mmol, 89%) as orange solid; mp 208-210 °C (EtOAc/hexanes); [α]_D²⁰ -214 (*c* 1.4, CHCl₃); IR (KBr) ν_{max} 3406, 3333, 3091, 2919, 2852, 1716, 1602, 1484, 1435 cm⁻¹; ¹H NMR (300 MHz, CDCl₃, rotameric) δ 6.17 (b, 1H), 5.06 (b, 1H), 4.86 (m, 0.5 H), 4.79 (m, 0.5H) 4.18-4.16 (m, 1H), 4.12 (s, 5H), 4.09-4.04 (m, 1H), 3.89-3.85 (m, 1H), 3.62-3.52 (m, 2H), 3.53-3.37 (m, 2H), 2.05-1.85 (m, 3H), 1.64-1.53 (m, 1H), 0.29 (s, 9H); ¹³C NMR (75.5 MHz, CDCl₃, rotameric) δ 157.5, 157.3, 99.5, 98.9, 70.4, 70.0, 68.1, 67.8, 67.7, 67.5, 66.9, 65.9, 65.1, 60.5, 47.0, 46.9, 28.6, 28.5, 24.2, 24.1, 0.06, 0.01; EIMS [*m/z* (%)] 400 (M⁺, 12), 300 (23), 299 (100), 121 (23), 70 (47); HRMS (EI) calcd for C₁₉H₂₈N₂O₂Si⁵⁶Fe: 400.1269; found 400.1263.

Aminoferrocene (CAS #1273-82-1) (189a**).**²⁵



A solution of **191a** (20.0 mg, 0.06 mmol) and aq. 6M KOH (0.5 mL) in 1,4-dioxane (0.5 mL) was heated at reflux for 22 h. After cooling to room temperature, 1,4-dioxane was removed under reduced pressure, and the aqueous phase was diluted with brine, extracted with dichloromethane (2×2 mL). The combined organic extract was dried over anhydrous Na_2SO_4 , filtered and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 50:45:5 EtOAc/hexanes/ Et_3N , $R_f = 0.43$) afforded **189a** (7 mg, 0.03 mmol, 58%) as orange glass; IR (KBr) ν_{max} 3389, 3323, 3207, 3277, 2923, 1612, 1496, 1405 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 4.10 (s, 5H), 3.99 (s, 2H), 3.84 (s, 2H), 2.59 (b, 2H). All other spectroscopic data were found to be in agreement with published data.²⁵

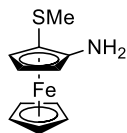
(-)-2S_p-Methyl-1-aminoferrocene (189b**).**



A solution of **191b** (20.0 mg, 0.06 mmol) and 50% (w/w) aq. NaOH (0.2 mL) in MeOH (0.6 mL) was heated at reflux for 20 h. After cooling to room temperature, the methanol was removed under reduced pressure, and the aqueous phase was diluted with brine, extracted with dichloromethane (2×2 mL). The combined organic extract was dried over anhydrous Na_2SO_4 , filtered and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 50:45:5 EtOAc/hexanes/ Et_3N , $R_f = 0.43$) afforded sequentially **189b** as orange solid (8 mg, 0.04 mmol, 67%), and recovered **191b** (4 mg, 0.01 mmol, 20%); $[\alpha]_{\text{D}}^{20} -39$ (c 0.2, abs. EtOH) [lit.¹²⁰ $[\alpha]_{\text{D}}^{20} +41$ (c 0.2, abs. EtOH) for R_p -enantiomer]; IR (KBr) ν_{max} 3406, 3333, 3091, 2919, 2852, 1716, 1601, 1484 cm^{-1} ; ^1H NMR (600 MHz, C_6D_6) δ 3.90 (s, 5H), 3.75-3.72 (m, 2H), 3.66 (s, 1H), 1.86 (b, 2H), 1.71 (s, 3H); ^{13}C NMR (150.9 MHz, C_6D_6) δ 105.1,

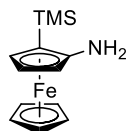
71.8, 69.8, 65.5, 60.8, 58.0, 30.2, 12.3; EIMS [m/z (%)] 215 (M^+ , 100), 149 (11), 93 (20), 56 (12); HRMS (EI) calcd for $C_{11}H_{13}N^{56}Fe$: 215.0397; found 215.0399.

(-)-2*R_p*-Thiomethyl-1-aminoferrocene (189c).



A solution of **191c** (48.0 mg, 0.13 mmol) and 50% (w/w) aq. NaOH (0.5 mL) in MeOH (1.5 mL) was heated at reflux for 20 h. After cooling to room temperature, the methanol was removed under reduced pressure, and the aqueous layer was diluted with brine, extracted with dichloromethane (2×2 mL), dried over anhydrous Na_2SO_4 , filtered and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 50:45:5 EtOAc/hexanes/ Et_3N , R_f = 0.50) afforded sequentially **189c** (10 mg, 0.04 mmol, 31%) as an orange glass, and recovered **191c** (25 mg, 0.07 mmol, 52%); $[\alpha]_D^{20}$ -83 (c 0.5, abs. EtOH); IR (KBr, neat) ν_{max} 3390, 3292, 3196, 2905, 2855, 1618, 1495, 1475 cm^{-1} ; 1H NMR (600 MHz, C_6D_6) δ 4.08 (s, 1H), 3.98 (m, 5H), 3.74-3.70 (m, 2H), 2.46 (b, 2H), 1.94 (s, 3H); ^{13}C NMR (150.9 MHz, C_6D_6 from HSQC & HMBC spectra) δ 109.3, 71.2, 70.3, 68.4, 62.9, 56.9, 19.7; EIMS [m/z (%)] 247 (M^+ , 100), 232 (31), 166 (62), 56 (12); HRMS (EI) calcd for $C_{11}H_{13}SN^{56}Fe$: 247.0118; found 247.0120.

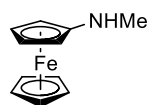
(-)-2*R_p*-Trimethylsilyl-1-aminoferrocene (189d).



A solution of **191d** (20.0 mg, 0.05 mmol) and aq. 6M KOH (0.5 mL) in 1,4-dioxane (0.5 mL) was heated at reflux for 22 h. After cooling to room temperature, dioxane was removed under reduced pressure, and the aqueous phase was diluted with brine, extracted with dichloromethane (2×2 mL). The combined organic extract was dried over anhydrous Na_2SO_4 , filtered and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 50:45:5

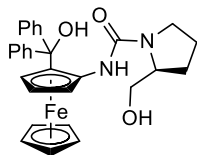
EtOAc/hexanes/Et₃N, $R_f = 0.65$) afforded sequentially **189d** (9 mg, 0.03 mmol, 65%) and an orange glass and recovered **191d** (3 mg, 0.01 mmol, 15%). $[\alpha]_D^{20} -44$ (c 0.2, abs. EtOH); IR (KBr) ν_{\max} 3423, 3350, 3216, 3093, 2953, 2895, 1613, 1463, 1431 cm^{-1} ; ¹H NMR (300 MHz, CDCl₃) δ 4.14 (s, 1H), 4.07 (s, 5H), 4.00 (s, 1H), 3.77 (s, 1H), 2.60 (b, 2H), 0.32 (s, 9H); ¹³C NMR (75.5 MHz, CDCl₃) δ 110.4, 69.0, 68.9, 65.6, 61.5, 59.7, 0.01; EIMS [m/z (%)] 273 (M^+ , 100); HRMS (EI) calcd for C₁₃H₁₉NSi⁵⁶Fe: 273.0636; found 273.0639.

***N*-Methyl aminoferrocene (189e).**



To a solution of **191a** (108 mg, 0.33 mmol) in THF (5 mL) was added LiAlH₄ (62.0 mg, 1.64 mmol) at 0 °C and was then heated to reflux for 16 h. After cooling to 0 °C, work up was carried out using Fieser's method and the volatiles were concentrated and purified using flash column chromatography (silica gel, 50:46:4 EtOAc/hexanes/Et₃N, $R_f = 0.50$) afforded **189e** (36 mg, 0.17 mmol, 51%) as an orange solid; mp 51-52 °C; IR (neat) ν_{\max} 3364, 3348, 3326, 3086, 2920, 2804, 1503, 1443 cm^{-1} ; ¹H NMR (300 MHz, CDCl₃) δ 4.16 (s, 5H), 3.89 (s, 4H), 2.73 (s, 3H), 2.31 (b, 1H); ¹³C NMR (75.5 MHz, CDCl₃) δ 112.1, 67.8, 63.0, 55.4, 33.8; EIMS [m/z (%)] 215 (M^+ , 100), 200 (24), 121 (37), 93 (17), 66 (11); HRMS (EI) calcd for C₁₁H₁₃N⁵⁶Fe: 215.0392; found 215.1391.

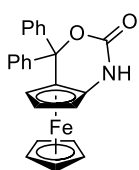
(-)-2*S*-Hydroxymethylpyrrolidine-1-carbox-[2*R_p*-(iodo)ferrocenyl]-amide (191e).



A mixture of **188g** (233 mg, 0.38 mmol) and K₂CO₃ (311 mg, 2.25 mmol) in MeOH (5 mL) was heated to reflux for 30 min.. After cooling to room temperature, the mixture was passed through Celite, rinsed well with CH₂Cl₂ and concentrated under reduced pressure. The crude hemiaminal

was redissolved in abs. EtOH (5 mL), treated with NaBH₄ (85.0 mg, 2.25 mmol), and heated to reflux for another 30 min.. After cooling to 0 °C, workup was performed by careful addition of sat. aq. NH₄Cl (2 mL). The excess EtOH was evaporated under reduced pressure and the mixture was extracted with CH₂Cl₂ (2 × 20 mL), washed with H₂O, brine, dried over anhydrous Na₂SO₄ and was concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 50:46:4 EtOAc/hexanes/Et₃N, *R_f* = 0.18) afforded **191e** (175 mg, 0.34 mmol, 92%) as orange glass; [α]_D²⁰ -255 (*c* 1.1, CHCl₃); IR (KBr) ν_{max} 3317, 3084, 2951, 2926, 2872, 1632, 1547, 1491, 1393 cm⁻¹; ¹H NMR (300 MHz, CD₃OD, rotameric) δ 7.49-7.46 (d, 2H, *J* = 7.2 Hz), 7.37-7.28 (m, 3H), 7.23-7.19 (m, 3H), 7.13-7.10 (m, 2H), 5.09 (s, 1H), 4.16 (s, 5H), 4.00 (s, 1H), 3.77-3.53 (m, 1H), 3.52-3.48 (m, 1H), 3.40-3.30 (m, 2H), 3.26-3.22 (m, 1H), 3.10-3.09 (m, 1H), 1.91-1.79 (m, 4H); ¹³C NMR (75.5 MHz, CD₃OD, rotameric) δ 157.3, 148.0, 147.6, 128.7, 128.7, 128.5, 128.2, 128.1, 87.1, 80.3, 70.8, 67.3, 67.2, 64.9, 64.7, 64.4, 63.9, 63.8, 60.2, 47.5, 28.9, 28.7, 24.5, 24.4; EIMS [*m/z* (%)] 510 (M⁺, 1.2), 393 (19), 367 (17), 365 (28), 363 (32); HRMS (EI) calcd for C₂₉H₃₀N₂O₃Fe: 510.1605; found 510.1599.

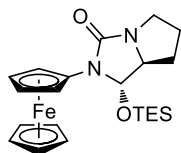
(+)-2R_p-4,4-Diphenyl-ferrocenyl[1,3]oxazin-2-one (193).



A solution of **190e** (66.0 mg, 0.03 mmol) and aq. 50% w/w NaOH (1.0 mL) in MeOH (0.5 mL) was heated at reflux for 6 h. After cooling to room temperature, 1,4-dioxane was removed under reduced pressure, and the aqueous phase was diluted with brine, extracted with dichloromethane (2 × 2 mL). The combined organic extract was dried over anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 50:45:5 EtOAc/hexanes/Et₃N, *R_f* = 0.40) afforded **193** (17 mg, 0.04 mmol, 32%) as an orange

glassy solid; $[\alpha]_D^{20} +584$ (c 0.4, CHCl_3); IR (CHCl_3) ν_{max} 3437, 3065, 3032, 3011, 2960, 2933, 1709, 1625, 1494 cm^{-1} ; ^1H NMR (600 MHz, C_6D_6) δ 8.33-8.30 (bs, 1H), 7.60 (d, 2H, $J = 7.2$ Hz), 7.29 (d, 2H, $J = 6.6$ Hz), 7.16-7.12 (m, 2H), 7.05 (t, 1H, $J = 7.8$ Hz), 6.91 (m, 3H), 4.04 (m, 1H), 3.97 (s, 5H), 3.75-3.74 (m, 1H), 3.65 (t, 1H, $J = 7.8$ Hz); ^{13}C NMR (75.5 MHz, CDCl_3) δ 153.0, 142.8, 142.4, 128.4, 128.1, 127.9, 127.4, 127.3, 125.4, 94.2, 87.3, 77.4, 70.0, 63.3, 62.4, 56.2; EIMS [m/z (%)] 409 (M^+ , 8), 245 (29), 244 (100), 120 (18), 83 (86); HRMS (EI) calcd for $\text{C}_{24}\text{H}_{19}\text{NO}_2^{56}\text{Fe}$: 409.0765; found 409.0760.

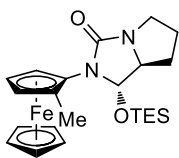
(-)-2-Ferrocenyl-1*S*-triethylsilyloxy-7*aS*-hexahydropyrrolo[1,2-*c*]imidazol-3-one
(*anti*-**187**).



Hydantoin **185** (3.00 g, 9.25 mmol) and Schwartz's reagent (3.10 g, 12.03 mmol) were suspended in THF (70 mL) and stirred at room temperature. After 10 min., TLC (3:7 EtOAc/hexanes, $R_f = 0.06$) indicated consumption of starting material. The reaction mixture was worked up with saturated aqueous NaHCO_3 solution followed by water (10 mL). The reaction mixture was filtered through Celite using copious CH_2Cl_2 and concentrated under reduced pressure to afford a mixture of hemiaminals (3.02 g) that should be protected within 2 h. A solution of the hemiaminals (**186**, 3.02 g) in THF (70 mL) was cooled to 0 °C and treated with *n*-BuLi (4.01 mL, 2.31 M in hexanes, 9.27 mmol). A distinct color change from orange to red-orange was observed. After 3 min., TESC1 (2.02 mL, 12.05 mmol) was added drop-wise and the mixture was stirred for an additional 5 min., wherein a distinct color change from red-orange to orange was observed. After 10 min., the reaction mixture was removed from the ice bath, allowed to warm to room temperature before being diluted with diethyl ether (20 mL), and worked up with water (5 mL). After

extraction of the reaction mixture with diethyl ether (3×10 mL), the combined organic extract was dried over anhydrous Na_2SO_4 , filtered and concentrated under reduced pressure to give **187** (3.2 g, 7.3 mmol, 92%) as a 0.95:1 mixture of *anti*/*syn* epimers. Purification by flash column chromatography (silica gel, 1:9 EtOAc/hexanes, R_f (*syn*) = 0.16, R_f (*anti*) = 0.20) separated *anti*-**187** and *syn*-**187**. Recrystallization of the chromatographed *anti* epimer from EtOH-water afforded *anti*-**187** (1.5 g, 3.4 mmol, 42%) in two crops as a diastereomerically enriched crystalline orange solid. Recrystallization of the chromatographed *syn* epimer from EtOH-water afforded *syn*-**187** (1.6 g, 3.6 mmol, 44%) as a diastereomerically enriched crystalline orange solid for an overall yield of 86% (3 g). The following data were obtained for *anti*-**187**: mp 80-81 °C (EtOH/water); $[\alpha]_D^{20}$ -67 (c 1.0, CHCl_3); CSP HPLC analysis (Chiralcel OD-H; eluent: 97:3 hexanes/*i*-PrOH, 1.0 mL/min) determined >99:1 er, >98% ee [t_R (major) = 7.94 min, t_R (minor) = 14.92 min]; IR (KBr) ν_{max} 3091, 3081, 2954, 2897, 2873, 1693, 1504, 1417, 1092 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 5.39 (s, 1H), 4.95 (s, 1H), 4.43 (s, 1H), 4.17 (s, 5H), 4.02 (s, 1H), 3.96 (s, 1H), 3.79-3.70 (m, 1H), 3.44-3.39 (m, 1H), 3.15-3.07 (m, 1H), 2.10-1.84 (m, 3H), 1.31-1.22 (m, 1H), 1.00 (t, 9H, J = 7.8 Hz), 0.69 (q, 6H, J = 7.8 Hz); ^{13}C NMR (150.9 MHz, CDCl_3) δ 160.6, 96.7, 84.5, 68.8, 66.8, 64.4, 63.9, 61.2, 59.1, 45.5, 28.6, 24.8, 6.8, 5.2; EIMS [m/z (%)] 440 (M^+ , 18), 308 (57), 243 (90), 103 (100), 75 (81), 47 (20); HRMS (EI) calcd for $\text{C}_{22}\text{H}_{32}\text{N}_2\text{O}_2\text{Si}^{56}\text{Fe}$: 440.1582; found 440.1575; Anal. calcd for $\text{C}_{22}\text{H}_{32}\text{N}_2\text{O}_2\text{SiFe}$: C, 59.99; H, 7.32. Found: C, 60.17; H, 7.21.

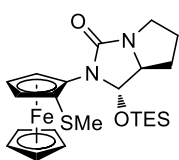
(–)-2-[(2*R*_p-Methyl)ferrocenyl]-1*S*-triethylsilyloxy-7*aS*-hexahydropyrrolo[1,2-*c*]imidazol-3-one (190a**).**



A solution of *anti*-**187** (100 mg, 0.22 mmol) in THF (2 mL) at $-78\text{ }^{\circ}\text{C}$ was exposed to *t*-BuLi (0.49 mL, 1.01 M in pentane, 0.50 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with MeI (0.03 mL, 0.57 mmol) and stirred for 10 min. at that temperature. Workup was conducted by addition of water (0.5 mL), brine (5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether ($3 \times 10\text{ mL}$). The combined organic extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.44$) afforded **190a** (92 mg, 0.20 mmol, 89%) as a diastereomerically enriched orange solid ($>95:5$ dr by NMR); mp $128\text{--}129\text{ }^{\circ}\text{C}$ (EtOH/ H_2O); $[\alpha]_{\text{D}}^{20} -132$ ($c\text{ }1.0$, CHCl_3); X-Ray diffractometry was performed on an orange plate ($0.12 \times 0.12 \times 0.04\text{ mm}^3$): $\text{C}_{23}\text{H}_{34}\text{N}_2\text{O}_2\text{SiFe}$: $M = 454.46\text{ g/mol}$, orthorhombic, $P2_12_12_1$, $a = 7.4514(2)\text{ \AA}$, $b = 15.7850(5)\text{ \AA}$, $c = 19.2930(7)\text{ \AA}$, $V = 2269.25(13)\text{ \AA}^3$, $\alpha = 90^{\circ}$, $\beta = 90^{\circ}$, $\gamma = 90^{\circ}$, $Z = 4$, $D_c = 1.330\text{ g/cm}^3$, $F(000) = 968$, $T = 147(2)\text{ K}$; 13733 reflections were collected. The structure was solved by Direct Methods (SHELXTL) and refined by full-matrix least squares on F^2 resulting in final R , R_w and GOF [for 3738 data with $F > 2\sigma(F)$] of 0.0492, 0.1354 and 1.040, respectively, for solution using the R_p enantiomer model [Flack parameter = 0.021(7)] [Crystallographic data (excluding structure factors) for **190a** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 915630]; IR (KBr) ν_{max} 2956, 2918, 2875, 1714, 1487, 1392, 1190, 1072, 1009 cm^{-1} ; ^1H NMR (300 MHz,

CDCl₃) δ 5.32 (s, 1H), 4.17 (s, 5H), 4.05 (m, 2H), 3.91 (t, 1H, $J = 2.4$ Hz), 3.76-3.70 (m, 1H), 3.43-3.38 (m, 1H), 3.14-3.08 (m, 1H), 2.07-1.92 (m, 2H), 1.92 (s, 3H), 1.93-1.83 (m, 1H), 1.43-1.36 (m, 1H), 0.93 (t, 9H, $J = 7.8$ Hz), 0.62-0.54 (m, 6H); ¹³C NMR (150.9 MHz, CDCl₃) δ 161.1, 93.7, 86.7, 81.3, 69.6, 67.2, 66.7, 63.9, 63.3, 45.8, 27.8, 24.9, 13.4, 6.8, 5.1; EIMS [m/z (%)] 454 (M^+ , 18), 322 (81), 257 (100), 241 (21), 121 (32), 103 (99), 75 (92), 56 (34); HRMS (EI) calcd for C₂₃H₃₄N₂O₂Si⁵⁶Fe: 454.1739; found 454.1735; Anal. calcd for C₂₃H₃₄N₂O₂SiFe: C, 60.79; H, 7.54. Found: C, 60.81; H, 7.46.

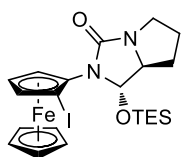
(-)-2-[(2*S*_p-Thiomethyl)ferrocenyl]-1*S*-triethylsilyloxy-7*aS*-hexahydropyrrolo[1,2-*c*]imidazol-3-one (190b**).**



A solution of *anti*-**187** (100 mg, 0.22 mmol) in THF (2 mL) at -78 °C was exposed to *t*-BuLi (0.36 mL, 1.40 M in pentane, 0.50 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with (MeS)₂ (0.05 mL, 0.57 mmol) and stirred for 30 min. at that temperature. Workup was conducted by addition of water (0.5 mL), brine (5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether (3×10 mL). The combined organic extract was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 10:86:4 EtOAc/hexanes/Et₃N, $R_f = 0.45$) afforded **190b** (105 mg, 0.22 mmol, 95%) as a diastereomerically enriched dark-orange oil; $[\alpha]_D^{20} -216$ (c 1.1, CHCl₃); IR (KBr, neat) ν_{\max} 3090, 2953, 2921, 2876, 1720, 1479, 1401, 1066 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.56 (s, 1H), 4.37-4.36 (m, 1H), 4.29 (s, 5H), 4.28-4.26 (m, 1H), 4.18 (t, 1H, $J = 2.7$ Hz), 3.75-3.69 (m, 1H), 3.48-3.43 (m, 1H), 3.11-3.05 (m, 1H), 2.19 (s, 3H), 2.05-1.99 (m, 2H), 1.90-1.75 (m, 1H), 1.70-1.60 (m, 1H), 0.97 (t, 9H, J

= 7.8 Hz), 0.67 (q, 6H, J = 7.8 Hz); ^{13}C NMR (150.9 MHz, CDCl_3) δ 162.6, 95.8, 88.1, 80.0, 70.8, 70.5, 67.5, 66.6, 65.9, 46.0, 28.2, 24.8, 20.3, 6.9, 5.6; EIMS [$m/z(\%)$] 486 (M^+ , 100), 454 (70), 289 (21), 273 (74), 103 (68), 75 (57); HRMS (EI) calcd for $\text{C}_{23}\text{H}_{34}\text{N}_2\text{O}_2\text{SSi}^{56}\text{Fe}$: 486.1459; found 486.1457.

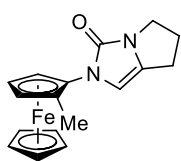
(-)-2-[(2*S*_p-Iodo)ferrocenyl]-1*S*-triethylsilyloxy-7*aS*-hexahydro-pyrrolo[1,2-*c*]imidazol-3-one (190c**).**



A solution of *anti*-**187** (100 mg, 0.22 mmol) in THF (2 mL) at $-78\text{ }^\circ\text{C}$ was exposed to *t*-BuLi (0.36 mL, 1.40 M in pentane, 0.50 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with a solution of $\text{ICH}_2\text{CH}_2\text{I}$ (160 mg, 0.57 mmol) in THF (3 mL) and stirred for 45 min. at that temperature. Workup was conducted by addition of water (0.5 mL), brine (5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether ($3 \times 10\text{ mL}$). The combined organic extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, R_f = 0.45) afforded **190c** (120 mg, 0.21 mmol, 93%) as a diastereomerically enriched dark-orange oil; $[\alpha]_D^{20}$ -135 (c 1.3, CHCl_3); IR (KBr, neat) ν_{max} 3091, 2954, 2910, 2875, 1722, 1475, 1398, 1072, 1005 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 5.43 (s, 1H), 4.45 (t, 1H, J = 2.1 Hz), 4.30 (s, 5H), 4.20 (m, 2H), 3.79-3.72 (m, 1H), 3.50-3.42 (m, 1H), 3.13-3.06 (m, 1H), 2.08-2.00 (m, 2H), 1.89-1.86 (m, 1H), 1.67-1.59 (m, 1H), 0.96 (t, 9H, J = Hz), 0.63 (q, 6H, J = 7.8 Hz); ^{13}C NMR (75.5 MHz, CDCl_3) δ 161.4 95.4, 87.3, 72.6, 72.2, 67.0, 66.5, 66.3, 45.8, 42.1, 28.2, 24.9, 6.9, 5.4; EIMS [$m/z(\%)$] 566 (M^+ , 58), 434 (19), 252 (36),

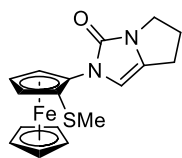
149 (100), 103 (67), 75 (57), 57 (29); HRMS (EI) calcd for C₂₂H₃₁IN₂O₂Si⁵⁶Fe: 566.0549; found 566.0534.

(+)-2-[(2*R*_p-Methyl)ferrocenyl]-2,5,6,7-tetrahydropyrrolo[1,2-*c*]-imidazol-3-one (*ent*-192a**).**



A solution of **190a** (39.0 mg, 0.09 mmol) and *p*-toluenesulfonic acid monohydrate (65.0 mg, 0.34 mmol) in CHCl₃ (1 mL) was heated to reflux for 40 min.. The solution was cooled to room temperature, diluted with chloroform (10 mL) and was washed sequentially with sat. aq. NaHCO₃, H₂O, brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, EtOAc, *R*_f = 0.32) afforded *ent*-**192a** (26 mg, 0.08 mmol, 95%) as an enantiomerically enriched orange solid that could be recrystallized from EtOH/water; mp 135-136 °C (EtOH/water); [α]_D²⁰ +31.0 (*c* 1.3, CHCl₃) [*S*_p enantiomer [α]_D²⁰ -29 (*c* 1.0, CHCl₃)]; CSP HPLC analysis (Chiralcel OD-H; eluent: 50:50 hexanes/*i*-PrOH, 1.0 mL/min) determined 97:3 er, 94% ee [*t*_R(minor) = 6.39 min, *t*_R(major) = 8.58 min]; Spectroscopic data matched that for antipode **192a**: IR (KBr) ν_{max} 3126, 3077, 2954, 2883, 2852, 1678, 1630, 1493, 1408 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.33 (s, 1H), 4.38 (m, 1H), 4.20 (s, 5H), 4.11 (m, 1H), 4.02 (m, 1H), 3.76 (b, 2H), 2.79 (bt, 2H), 2.43 (m, 2H), 2.03 (s, 3H).

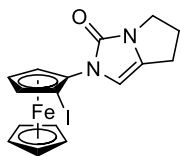
(+)-2-[2*S*_p-(Thiomethyl)ferrocenyl]-2,5,6,7-tetrahydropyrrolo[1,2-*c*]imidazol-3-one (*ent*-192b**).**



A solution of **190b** (99.0 mg, 0.20 mmol) and *p*-toluenesulfonic acid monohydrate (154 mg, 0.81 mmol) in CHCl₃ (3 mL) was heated to reflux for 40 min.. The solution was cooled to room temperature,

diluted with chloroform (10 mL) and was washed sequentially with sat. aq. NaHCO₃, H₂O, brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, EtOAc, R_f = 0.24) afforded *ent*-**192b** (66 mg, 0.15 mmol, 92%) as an orange oil; $[\alpha]_D^{20}$ +136 (c 1.0, CHCl₃) [R_p enantiomer -129 (c 1.0 CHCl₃)]; CSP HPLC analysis (Chiralcel OD-H; eluent: 70:30 hexanes/*i*-PrOH, 1.0 mL/min) determined 95.5:4.5 er, 91% ee [t_R (minor) = 7.93 min, t_R (major) = 10.69 min]; Spectroscopic data matched for antipode **192b**: IR (KBr, neat) ν_{\max} 3154, 3092, 2979, 2919, 1690, 1639, 1487, 1409, 1114 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.75 (s, 1H), 4.90 (m, 1H), 4.26-4.25 (m, 1H), 4.22 (s, 5H), 4.17 (t, 1H, J = 2.7 Hz), 3.70 (t, 2H, J = 6.9 Hz), 2.76 (t, 2H, J = 6.9 Hz), 2.41 (quin, 2H, J = 6.9 Hz), 2.16 (s, 3H); EIMS [m/z (%)] 354 (M^+ , 23), 85 (65), 83 (100), 47 (21); HRMS (EI) calcd for C₁₇H₁₈N₂OS⁵⁶Fe: 354.0489; found 354.0491.

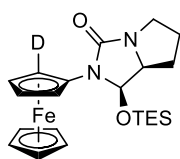
(+)-2-[2*S_p*-(Iodo)ferrocenyl]-2,5,6,7-tetrahydropyrrolo[1,2-*c*]imidazol-3-one(*ent*-192c**).**



A solution of **190c** (120 mg, 0.21 mmol) and *p*-toluenesulfonic acid monohydrate (161 mg, 0.85 mmol) in CHCl₃ (2 mL) was heated to reflux for 30 min.. The reaction mixture was cooled to room temperature, diluted with chloroform (10 mL) and was washed sequentially with sat. aq. NaHCO₃, H₂O, brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 80:15:5 EtOAc/hexanes/Et₃N, R_f = 0.22) afforded *ent*-**192c** (79 mg, 0.22 mmol, 85%) as a viscous orange oil; $[\alpha]_D^{20}$ +40 (c 1.1, CHCl₃) [R_p enantiomer $[\alpha]_D^{20}$ -38.9 (c 0.4, CHCl₃)]; CSP HPLC analysis (Chiralcel OD-H; eluent: 80:20 hexanes/*i*-PrOH, 1.0 mL/min) determined

99:1 er, 98% ee [$t_R(\text{minor}) = 12.51$ min, $t_R(\text{major}) = 13.46$ min]; Spectroscopic data matched for antipode **192c**: IR (KBr, neat) ν_{max} 3153, 3092, 2961, 2901, 1681, 1639, 1488, 1409, 1347, 1107 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 6.55 (s, 1H), 4.78 (m, 1H), 4.40 (m, 1H), 4.25 (s, 6H), 3.75 (t, 2H, $J = 6.3$ Hz), 2.80 (t, 2H, $J = 6.9$ Hz), 2.42 (quin, 2H, $J = 6.6$ Hz); EIMS [m/z (%)] 434 (M^+ , 17), 308 (50), 243 (57), 87 (93), 83 (53), 49 (100), 43 (98); HRMS (EI) calcd for $\text{C}_{16}\text{H}_{15}\text{IN}_2\text{O}^{56}\text{Fe}$: 433.9578; found 433.9570.

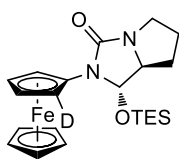
(+)-2-[(2*S_p*-Deutero)ferrocenyl]-1*R*-triethylsilyloxy-7*aS*-hexahydropyrrolo[1,2-*c*]imidazol-3-one (2*S_p*-D-*syn*-188i**).**



A solution of *syn*-**187** (200 mg, 0.45 mmol) in THF (4.5 mL) at -78 °C was exposed to *t*-BuLi (1.02 mL, 0.99 M in pentane, 1.00 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with methanol- d_4 (0.04 mL, 1.14 mmol) and stirred for 30 min. at that temperature. Workup was conducted by addition of water (0.5 mL), brine (5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether (3×10 mL). The combined organic extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 30:70 EtOAc/hexanes) afforded 2*S_p*-D-*syn*-**188i** (188 mg, 0.43 mmol, 94%) as a diastereomerically enriched orange solid. mp $94\text{--}95$ °C (EtOH, H_2O); $[\alpha]_{\text{D}}^{20} +124$ (c 1.0, CHCl_3); IR (KBr) ν_{max} 3084, 2953, 2910, 2875, 1687, 1493, 1410, 1084 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 5.41 (d, 1H, $J = 6.3$ Hz), 4.28 (s, 1H), 4.17 (s, 5H), 4.02 (s, 1H), 3.92–3.87 (m, 2H), 3.63–3.55 (m, 1H), 3.12–3.04 (m, 1H), 1.95–1.83 (m, 3H), 1.74–1.69 (m, 1H), 0.87 (t, 9H, $J = 8.1$ Hz), 0.56 (q, 6H, $J = 8.1$ Hz); ^{13}C NMR (150.9 MHz, CDCl_3) δ 159.0, 96.6, 82.4, 69.0, 65.0, 63.5, 61.8, 61.33 (t, $J = 27.9$

Hz), 61.31, 45.6, 26.3, 25.1, 6.6, 4.8; EIMS [m/z (%)] 441 (M^+ , 42), 309 (65), 244 (94), 228 (36), 103 (100), 75 (81); HRMS (EI) calcd for $C_{22}H_{31}DN_2O_2Si^{56}Fe$: 441.1645; found 441.1637.

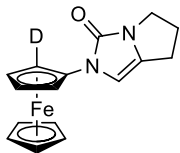
(–)-2-[(2*R_p*-Deutero)ferrocenyl]-1*S*-triethylsilyloxy-7*aS*-hexahydropyrrolo[1,2-*c*]imidazol-3-one (2*R_p*-D-*anti*-190d).



A solution of *anti*-**187** (68.0 mg, 0.15 mmol) in THF (2 mL) at $-78\text{ }^{\circ}\text{C}$ was exposed to *t*-BuLi (0.32 mL, 1.07 M in pentane, 0.34 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with methanol- d_4 (0.02 mL, 0.39 mmol) and stirred for 30 min. at that temperature. Workup was conducted by addition of water (0.5 mL), brine (5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether (3×10 mL). The combined organic extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 30:70 EtOAc/hexanes) afforded 2*R_p*-D-*anti*-**190d** (63.0 mg, 0.14 mmol, 93%) as a diastereomerically enriched orange solid. mp $75\text{--}76\text{ }^{\circ}\text{C}$ (EtOH/ H_2O); $[\alpha]_D^{20} -68$ (c 1.1, $CHCl_3$); IR (KBr) ν_{max} 3091, 3082, 2954, 2897, 2873, 1693, 1496, 1414, 1090 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 5.40 (s, 1H), 4.45 (s, 1H), 4.15 (s, 5H), 4.05 (s, 1H), 3.98 (s, 1H), 3.78–3.69 (m, 1H), 3.43–3.38 (m, 1H), 3.15–3.07 (m, 1H), 2.07–1.97 (m, 2H), 1.87–1.77 (m, 1H), 1.30–1.23 (m, 1H), 0.97 (t, 9H, $J = 7.8$ Hz), 0.68 (m, 6H, $J = 7.8$ Hz); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 160.4, 97.2, 84.5, 68.9, 66.7, 64.5, 63.9, 61.0 (t, $J = 27.2$ Hz), 59.0, 45.4, 28.5, 24.7, 6.8, 5.2; EIMS [m/z (%)] 441 (M^+ , 15), 309 (71), 244 (97), 103 (100), 75 (77), 47 (19); HRMS (EI) calcd for $C_{22}H_{31}DN_2O_2Si^{56}Fe$: 441.1645; found 441.1641.

(+)-2-[(2S_p-Deutero)ferrocenyl]-2,5,6,7-tetrahydropyrrolo[1,2-c]imidazol-3-one

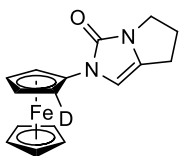
(192d).



A solution of **188i** (178 mg, 0.40 mmol) and *p*-toluenesulfonic acid monohydrate (307 mg, 1.61 mmol) in CHCl₃ (4 mL) was heated to reflux for 30 min.. The solution was cooled to room temperature, diluted with chloroform (10 mL) and was washed sequentially with sat. aq. NaHCO₃, H₂O, brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, EtOAc, *R_f* = 0.20) afforded **192d** (112 mg, 0.36 mmol, 90%) as an orange solid; $[\alpha]_D^{20} +4$ (*c* 1.0, CHCl₃); mp 190-191 °C IR (KBr) ν_{\max} 3105, 3051, 2981, 2952, 2889, 1678, 1633, 1498, 1458, 1413 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.13 (s, 1H), 4.70 (s, 1H), 4.19 (s, 5H), 4.07 (s, 2H), 3.74 (m, 2H), 2.75 (t, 2H, *J* = 6.6 Hz), 2.40 (m, 2H) EIMS [*m/z*(%)]⁺; ¹³C NMR (75.5 MHz, CDCl₃) δ 149.5, 126.9, 101.7, 94.9, 69.0, 64.7, 60.8, 60.7 (t, *J* = 27.2 Hz), 42.1, 27.8, 22.7; EIMS [*m/z* (%)] 309 (M⁺, 82), 308 (58), 245 (21), 244 (100), 243 (74), 50 (27); HRMS (EI) calcd for C₁₆H₁₅DN₂O⁵⁶Fe: 309.0674; found 309.0672.

(-)-2-[(2R_p-Deutero)ferrocenyl]-2,5,6,7-tetrahydropyrrolo[1,2-c]imidazol-3-one

(*ent*-192d).

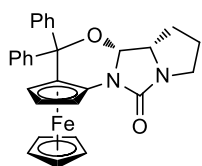


A solution of **190d** (58.0 mg, 0.13 mmol) and *p*-toluenesulfonic acid monohydrate (100 mg, 0.52 mmol) in CHCl₃ (2 mL) was heated to reflux for 30 min.. The solution was cooled to room temperature, diluted with chloroform (10 mL) and was washed sequentially with sat. aq. NaHCO₃, H₂O, brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by

flash column chromatography (silica gel, EtOAc, R_f = 0.20) afforded *ent*-**192d** (38 mg, 0.12 mmol, 94%) as an orange solid; mp 189-190 °C $[\alpha]_D^{20}$ -4 (c 0.7, CHCl₃) [R_p enantiomer $[\alpha]_D^{20}$ +4 (c 1.0, CHCl₃)]; IR (KBr) ν_{\max} 3105, 2967, 2890, 2859, 1678, 1498, 1413, 1347, 1101 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.13 (t, 1H, J = 1.2 Hz), 4.69 (q, 1H, J = 2.1 Hz), 4.18 (s, 5H), 4.06 (d, 2H, J = 1.8 Hz), 3.71 (t, 2H, J = 6.9 Hz), 2.74 (t, 2H, J = 7.8 Hz), 2.44 (q, 2H, J = 6.9 Hz); ¹³C NMR (75.5 MHz, CDCl₃) δ 149.5, 126.9, 101.7, 94.9, 69.0, 64.7, 60.8, 60.7 (t, J = 27.2 Hz), 42.1, 27.8, 22.7; EIMS [m/z (%)] 309 (M^+ , 79), 308 (17), 245 (19), 154 (12), 57 (13), 56 (15); HRMS (EI) calcd for C₁₆H₁₅DN₂O⁵⁶Fe: 309.0674; found 309.0672.

To a solution of **188g** (212.0 mg, 0.34 mmol) in CHCl₃ (4 mL) was added *p*-toluenesulfonic acid monohydrate (129.0 mg, 0.68 mmol) in one portion. After stirring for 5 min, a distinct color change from orange to brown was observed. The solution was quenched with saturated aqueous NaHCO₃ (1 mL). The organic layer was washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to give **194** (117 mg, 70%) as a 4:1 mixture of *anti/syn* epimers. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, R_f (*syn*) = 0.43, R_f (*anti*) = 0.23) separated *syn*-**194** (21 mg, 0.04 mmol, 13%), and *anti*-**194** (96 mg, 0.20 mmol, 57%).

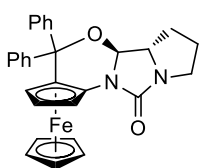
(+)-2-[(2*S*_p-5,5-Diphenyl-ferrocenyl)(6*aR*,6*bS*)-6*b*,7,8,9-tetrahydro-5*H*-pyrrolo [1',2':3,4]imidazo[5,1-*b*][1,3]oxazin-11(6*aH*)-one (syn-194).



The following data were obtained for *syn*-**194** (glassy solid): $[\alpha]_D^{20}$ +70 (c 0.8, CHCl₃); CSP HPLC analysis (Chiralcel OD-H; eluent: 80:20 hexanes/*i*-PrOH, 1.0 mL/min) determined >99:1 er, >98% ee [t_R (minor)

= 5.59 min, t_R (major) = 10.77 min]; IR (KBr) ν_{\max} 3085, 3058, 3026, 2954, 1714, 1504, 1402 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.50 (d, 2H, J = 7.5 Hz), 7.40 (t, 2H, J = 7.5 Hz), 7.31 (d, 1H, J = 6.9 Hz), 7.25-7.22 (m, 3H), 7.17-7.14 (m, 2H), 4.93 (d, 1H, J = 7.5 Hz), 4.69 (s, 1H), 4.16-4.07 (m, 2H), 3.87-3.74 (m, 7H), 3.19-3.11 (m, 1H), 2.36-2.28 (m, 1H), 2.182.12 (m, 2H), 1.98-1.93 (m, 1H); ^{13}C NMR (150.9 MHz, CDCl_3) δ 159.8, 146.3, 145.1, 128.0, 127.9, 127.8, 127.7, 126.7, 125.6, 94.1, 82.2, 80.5, 77.6, 69.8, 63.4, 62.7, 61.1, 56.0, 45.7, 25.4, 25.0; EIMS [m/z (%)] 490 (M^+ , 16), 105 (100), 84 (48), 77 (33), 49 (58); HRMS (EI) calcd for $\text{C}_{29}\text{H}_{26}\text{N}_2\text{O}_2^{56}\text{Fe}$: 490.1343; found 490.1345.

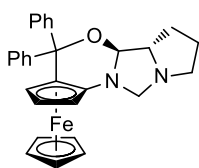
(+)-2-[(2*S*_p-5,5-Diphenyl-ferrocenyl)](6*aS*,6*bS*)-6*b*,7,8,9-tetrahydro-5*H*-pyrrolo [1',2':3,4]imidazo[5,1-*b*][1,3]oxazin-11(6*aH*)-one (*anti*-194**).**



The following data were obtained for *anti*-**194** (orange solid): mp 251-252 °C (CH_2Cl_2 /hexanes); $[\alpha]_D^{20}$ +168 (c 0.5, CHCl_3); CSP HPLC analysis (Chiralcel OD-H; eluent: 80:20 hexanes/*i*-PrOH, 1.0 mL/min) determined >99:1 er, >98% ee [t_R (minor) = 8.64 min, t_R (major) = 10.09 min]; IR (KBr) ν_{\max} 3085, 3058, 2968, 2896, 1712, 1502, 1392, 1028, 1001 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3) δ 7.74 (d, 2H, J = 7.8 Hz), 7.53 (t, 2H, J = 7.2 Hz), 7.43 (t, 1H, J = 7.2 Hz), 7.15-7.10 (m, 3H), 6.88-6.87 (m, 2H), 5.46 (s, 1H), 5.17 (s, 1H), 4.11 (t, 1H, J = 2.7 Hz), 3.90-3.85 (m, 2H), 3.70 (s, 5H), 3.68-3.63 (m, 1H), 3.18-3.14 (m, 1H), 2.23-2.18 (m, 1H), 2.11-2.07 (m, 1H), 1.99-1.94 (m, 1H), 1.58-1.52 (m, 1H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 158.7, 146.6, 144.9, 127.9, 127.7, 127.6, 127.5, 127.3, 126.4, 92.5, 83.1, 82.8, 80.7, 69.9, 64.2, 64.1, 63.5, 60.5, 45.3, 28.4, 25.7; EIMS [m/z (%)] 490 (M^+ , 8), 86 (64), 84 (100), 49 (17), 47 (19); HRMS (EI) calcd for $\text{C}_{29}\text{H}_{26}\text{N}_2\text{O}_2\text{Fe}$: 490.1343; found 490.1336. Anal. calcd for $\text{C}_{29}\text{H}_{26}\text{N}_2\text{O}_2^{56}\text{Fe}$: C, 71.03; H, 5.34. Found: C, 70.51; H, 5.14.

Scale-up: Repetition of the above procedure using **188g** (1.2 g, 1.90 mol) and *p*-toluenesulfonic acid monohydrate (716.0 mg, 3.76 mmol) in CHCl₃ (20 mL) afforded only *anti*-**194**. Following work up described above; the crude mixture was dissolved in minimum amount of CH₂Cl₂ and hexane was added to precipitate out orange solid which was recrystallized from CH₂Cl₂/hexanes in 70% yield (645 mg, 1.32 mmol).

(+)-2-[(2*S*_p-5,5-Diphenyl-ferrocenyl)](6*aS*,6*bS*)-6*a*,6*b*,7,8,9,11-hexahydro-5*H*-pyrrolo [1',2':3,4]imidazo[5,1-*b*][1,3]oxazine (195**).**

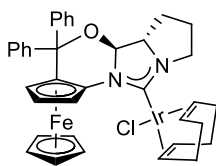


To a solution of *anti*-**194** (610 mg, 1.24 mmol) in THF (60 mL) at – 78 °C was added DIBAL-H (5.00 mL, 1.00 M solution in hexanes, 4.98 mmol). The reaction mixture was allowed to warm to room temperature overnight. After 16 h, the solution was cooled to 0 °C, diluted with EtOAc and quenched with sat. aq. potassium sodium tartrate (2 mL) and stirred for another 15 min. to separate organic and aqueous layers. The organic layer was washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 50:45:5 EtOAc/hexanes/Et₃N, *R_f* = 0.23) afforded **195** as orange crystalline solid (470 mg, 0.99 mmol, 79%); mp 203-204 °C; [α]_D²⁰ +312 (*c* 0.5, CHCl₃); IR (KBr) ν_{max} 3085, 3023, 2958, 2937, 2861, 2848, 1490, 1469, 1360, 1136, 1105 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.73 (d, 2H, *J* = 7.2 Hz), 7.45 (t, 2H, *J* = 7.2 Hz), 7.39 (t, 1H, *J* = 7.5 Hz), 7.12-7.09 (m, 3H), 6.96-6.93 (m, 2H), 4.89 (s, 1H), 4.45 (s, 1H), 3.99-3.97 (m, 1H), 3.89 (dd, 2H, *J* = 12.3 Hz, 6.9Hz), 3.84-3.80 (m, 2H), 3.68 (s, 5H), 3.21-3.22 (m, 1H), 2.88-2.87 (m, 1H), 2.25-2.24 (m, 1H), 1.86-1.77 (m, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 147.8, 146.0, 127.7, 127.5, 127.4, 127.1, 126.9, 126.6, 100.2, 91.2, 81.7, 81.4, 75.2, 70.2, 70.0, 63.9, 63.3, 61.9, 56.0, 20.6,

26.7; EIMS [m/z (%)] 476 (M^+ , 44), 83 (100), 55 (12); HRMS (EI) calcd for $C_{29}H_{28}N_2O_1Fe$: 476.1551; found 476.1554. Anal. calcd for $C_{29}H_{26}N_2O_2^{56}Fe$: C, 73.11; H, 5.92. Found: C, 72.81; H, 6.05.

(–)-Chloro[η^4 -1,5-cyclooctadiene]2-[2*S*_p-5,5-diphenyl-ferrocenyl](6*aS*,6*bS*)-

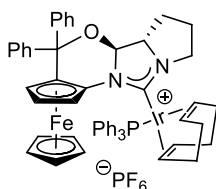
6*a*,6*b*,7,8,9,11-hexahydro-5*H*-pyrrolo[1',2':3,4]imidazol-2-ylidene]iridium (197**).**



A solution of **195** (200 mg, 0.42 mmol) and tritylium tetrafluoroborate (139 mg, 0.42 mmol) in CH_2Cl_2 (4 mL) was stirred in a Schlenk flask at room temperature covered from light. After 5 h, solvent was removed *in vacuo* and the crude solid was washed with dry diethyl ether (3 x 5 mL) and dried *in vacuo*. To this was added $Ir(\mu-Cl)(cod)]_2$ (141.0 mg, 0.21 mmol) and degassed THF (14 mL) in glovebox. The solution was cooled to $-78\text{ }^\circ\text{C}$ and with increased flow of argon, $KOtBu$ (47.0 mg, 0.42 mmol) was added at $-78\text{ }^\circ\text{C}$. After 1 h, the cold bath was removed and the volatiles were removed under reduced pressure. Purification of the residue by flash column chromatography (silica gel, 2:8 EtOAc/hexanes) afforded a 4:1 mixture of coordination isomers. The minor isomer was found to convert to major in $>95\%$ when stirred in CH_2Cl_2 for 16 h. Data for major isomer **197**: [194 mg, 0.24 mmol, 57%, $R_f = 0.25$ (2:8 EtOAc/hexanes)] as an orange crystalline solid; mp $222\text{--}223\text{ }^\circ\text{C}$ (CH_3CN); $[\alpha]_D^{20} -245$ (c 0.5, $CHCl_3$); X-Ray diffractometry was performed on an orange crystal ($0.16 \times 0.05 \times 0.04\text{ mm}^3$): $C_{37}H_{38}ClFeIrN_2O$: $M = 810.19\text{ g/mol}$, triclinic, $P1$, $a = 9.6609(9)\text{ \AA}$, $b = 11.9882(12)\text{ \AA}$, $c = 14.7752(14)\text{ \AA}$, $V = 1614.8(3)\text{ \AA}^3$, $\alpha = 74.139(2)^\circ$, $\beta = 89.285(2)^\circ$, $\gamma = 79.066(2)^\circ$, $Z = 2$, $D_c = 1.666\text{ g/cm}^3$, $F(000) = 804$, $T = 147(2)\text{ K}$; 26631 data were collected. The structure was solved by Direct Methods (SHELXTL) and refined by full-matrix least squares on F^2 resulting in final R , R_w and GOF [for 13430

data with $F > 2\sigma(F)$] of 0.0395, 0.0804 and 0.965, respectively, for solution using the *Sp* enantiomer model [Flack parameter = $-0.024(5)$]; [CCDC 1030224 contains the crystallographic data for **197**]; IR (KBr) ν_{\max} 2956, 2922, 2873, 2828, 1699, 1518, 1413 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.69 (d, 2H, $J = 7.5$ Hz), 7.52 (t, 2H, $J = 7.2$ Hz), 7.43 (t, 1H, $J = 7.2$ Hz), 7.16-7.11 (m, 3H), 6.88-6.84 (m, 2H), 6.28-6.27 (m, 1H), 5.73 (d, 1H, $J = 4.2$ Hz), 4.85-4.80 (m, 1H), 4.69-4.63 (m, 1H), 4.48-4.39 (m, 1H), 4.19 (t, 1H, $J = 2.7$ Hz), 4.05-3.98 (m, 1H), 3.93-3.91 (m, 1H), 3.78 (s, 5H), 3.54-3.46 (m, 1H), 3.24-3.20 (m, 1H), 2.87-2.81 (m, 1H), 2.36-2.15 (m, 12H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 206.4, 146.4, 144.8, 127.8, 127.7, 127.6, 127.4, 126.1, 93.9, 89.4, 86.5, 86.3, 83.6, 81.4, 70.63, 68.5, 64.6, 64.0, 63.0, 54.7, 51.1, 46.3, 34.0, 32.8, 29.6, 28.9, 28.5, 25.5; FABMS [m/z (%)] 810 (M^+ , 2), 95 (50), 91 (36), 67 (70), 55 (100), 43 (99), 39 (54), 29 (73); HRMS (FAB) calcd for $\text{C}_{37}\text{H}_{38}\text{N}_2\text{OClFeIr}$: 810.1651; found 810.1419. Anal. calcd for $\text{C}_{37}\text{H}_{38}\text{N}_2\text{OCl}^{56}\text{FeIr}$: C, 54.85; H, 4.73. Found: C, 54.57; H, 4.75.

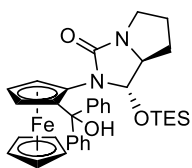
(–)-[η^4 -1,5-cyclooctadiene][triphenylphosphine]2-[2*S*_p-5,5-diphenyl-ferrocenyl] (6*aS*,6*bS*)6*a*,6*b*,7,8,9,11-hexahydro-5*H*-pyrrolo[1',2':3,4]imidazol-2-ylidene]iridium hexafluorophosphate (198**).**



To a solution of **197** (100 mg, 0.12 mmol) in CH_2Cl_2 (1 mL) was added a solution of triphenylphosphine (32.0 mg, 0.12 mmol) in CH_2Cl_2 (1 mL) and resulting red solution was stirred for 3 h at room temperature and then concentrated. The residue was dissolved in minimum amount of CH_3CN and KPF_6 (29.0 mg, 0.16 mmol) in CH_3CN was added and stirred at room temperature for another hour, passed through Celite and washed with CH_2Cl_2 . Volatiles were removed under reduced pressure and resulting red solid was triturated with pentane

to afford **198** as red crystalline solid (131 mg, 0.13 mmol, 90%). mp 189-190 °C; $[\alpha]_D^{20} - 72$ (*c* 0.5, CHCl₃); IR (KBr) ν_{\max} 2918, 2880, 2850, 1500, 1436, 838 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.57-7.52 (m, 14H), 7.41 (m, 4H), 7.33 (m, 2H), 7.16-7.14 (m, 3H), 6.91 (d, 2H, *J* = 6.3 Hz), 5.77 (s, 1H), 5.24 (s, 1H), 4.74 (m, 1H), 4.35 (s, 1H), 4.24 (m, 2H), 4.01 (m, 1H), 3.75 (m, 1H), 3.55-3.46 (m, 7H), 3.29-3.28 (m, 1H), 2.42-2.35 (m, 1H), 2.29-2.17 (m, 3H), 1.97-1.91 (m, 6H), 1.60-1.49 (m, 1H), 1.15-1.12 (m, 1H); ³¹P NMR (121.5 MHz, CDCl₃) 16.18 (s), -144.2 (septet, *J* = 713.2 Hz); ¹⁹F NMR (282.4 MHz, CDCl₃) -73.5 (d, *J* = 711.6 Hz); ¹³C NMR (75.5 MHz, CDCl₃) δ 202.9, 145.6 (d, *J* = 6.8 Hz), 133.7 (d, *J* = 19 Hz), 131.8, 129.2 (d, *J* = 9.8 Hz), 128.7, 128.4, 128.2, 128.0 (t, *J* = 9.1 Hz), 127.6, 125.5, 94.0, 90.5 (d, *J* = 8.3 Hz), 86.5, 85.1, 83.1, 81.4, 81.2, 80.7, 71.4, 70.2, 65.4, 64.1, 62.4, 45.2, 33.2, 32.2, 29.2, 29.0, 25.9, 24.8; FABMS [*m/z* (%)] 1037 (*M*⁺, 8), 83 (29), 71 (30), 69 (60), 67 (38), 55 (100), 43 (94); HRMS (FAB) calcd for C₅₅H₅₃N₂OPFeIr: 1037.2874; found 1037.2830. Anal. calcd for C₅₅H₅₃N₂OP⁵⁶FeIr⁺PF₆⁻: C, 55.89; H, 4.52. Found: C, 55.72; H, 4.66.

(-)-2-[(2*R*_p-(Diphenylhydroxymethyl)ferrocenyl]-1*S*-triethylsilyloxy-7*aS* hexahydro pyrrolo[1,2-*c*]imidazol-3-one (190e).

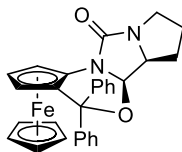


To a solution of *anti*-**187** (809 mg, 1.84 mmol) in THF (15 mL) at -78 °C was added *t*-BuLi (4.00 mL, 1.04 M in hexanes, 4.04 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched a solution of Ph₂CO (837 mg, 4.59 mmol) in THF (5 mL) and stirred for 30 min. at that temperature. Workup was conducted by addition of water (0.5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether (2 × 40 mL). The combined organic extract was washed

with water, brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 2:8 EtOAc/hexanes, R_f = 0.43) afforded **190e** (1.1 g, 1.80 mmol, 93%) as a diastereomerically enriched orange crystalline solid; mp 181-182 °C (EtOH/H₂O); $[\alpha]_D^{20}$ -67 (c 1.0, CHCl₃); IR (KBr) ν_{\max} 3221, 3086, 3054, 2954, 2909, 1686, 1460 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.74 (d, 2H, J = 7.2 Hz), 7.46 (d, 2H, J = 6.9 Hz), 7.31-7.29 (m, 1H), 7.23-7.14 (m, 5H), 5.37 (s, 1H), 4.40 (s, 5H), 4.31- 4.29 (m, 1H), 4.02 (t, 1H, J = 2.7 Hz), 3.45-3.43 (m, 1H), 3.38-3.29 (m, 1H), 3.23-3.18 (m, 1H), 2.96-2.90 (m, 1H), 1.82-1.81 (m, 1H), 1.74-1.66 (m, 2H), 0.97 (t, 10H, J = 7.8 Hz), 0.67 (q, 6H, J = 7.8 Hz); ¹³C NMR (75.5 MHz, CDCl₃) δ 161.5, 147.5, 145.9, 127.6, 127.3, 127.2, 127.1, 126.3, 126.2, 92.0, 90.8, 87.2, 76.1, 70.4, 70.1, 66.4, 66.0, 63.5, 45.3, 28.3, 24.9, 6.8, 5.2; EIMS [m/z (%)] 622 (M^+ , 3), 490 (56), 105 (58), 103 (100), 75 (79); HRMS (EI) calcd for C₃₅H₄₂N₂O₃Si⁵⁶Fe: 622.2314; found 622.2285. Anal. calcd for C₃₅H₄₂N₂O₃SiFe: C, 67.51; H, 6.80. Found: C, 67.25; H, 6.72.

To a solution of **190e** (1.10 g, 2.00 mmol) in CHCl₃ (20 mL) was added *p*-toluenesulfonic acid monohydrate (761 mg, 4.00 mmol). After stirring for 5 min, a distinct color change from orange to brown was observed. The solution was quenched with sat. aq. NaHCO₃. The organic layer was washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to give **199** (650 mg, 1.33 mmol, 66%) as a 1.4:1 mixture of *syn/anti* epimers. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, R_f (*anti*) = 0.32, R_f (*syn*) = 0.29) separated *syn*-**199** (380 mg, 0.77 mmol, 39%), and *anti*-**199** (270 mg, 0.55 mmol, 27%).

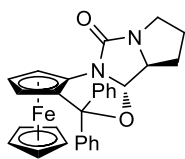
**(-)-2-[(2*R*_p-5,5-Diphenyl-ferrocenyl)](6*aR*,6*bS*)-6*b*,7,8,9-tetrahydro-5*H*-pyrrolo
[1',2':3,4]imidazo[5,1-*b*][1,3]oxazin-11(6*aH*)-one (*syn*-**199**).**



The following data were obtained for *syn*-**199** (orange solid): mp 97-98 °C; $[\alpha]_D^{20}$ -303 (*c* 1.0, CHCl₃); CSP HPLC analysis (Chiralcel OD-H; eluent: 60:40 hexanes/*i*-PrOH, 0.5 mL/min) determined >99:1

er, >98% ee [*t*_R(minor) = 10.85 min, *t*_R(major) = 11.56 min]; IR (KBr) ν_{\max} 3086, 3057, 3026, 2924, 2853, 1713, 1504, 1492, 1398 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.72 (d, 2H, *J* = 7.2 Hz), 7.52 (t, 2H, *J* = 7.8 Hz), 7.42 (t, 1H, *J* = 7.2 Hz), 7.14-7.08 (m, 3H), 6.87-6.84 (m, 2H), 5.58 (d, 1H, *J* = 6.6 Hz), 5.08-5.06 (m, 1H), 4.21-4.15 (m, 1H), 4.09 (t, 1H, *J* = 2.7 Hz), 3.81-3.79 (m, 1H), 3.75 (s, 5H), 3.73-3.67 (m, 1H), 3.14-3.06 (m, 1H), 2.14-2.08 (m, 1H), 1.91-1.83 (m, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 159.1, 146.9, 144.8, 127.7, 127.7, 127.6, 127.4, 127.3, 125.6, 93.1, 82.6, 80.9, 80.5, 70.0, 64.0, 60.4, 60.3, 46.2, 45.6, 26.5, 24.3; EIMS [*m/z*(%)] 490 (M⁺, 4), 87 (12), 85 (59), 83 (100), 47 (18); HRMS (EI) calcd for C₂₉H₂₆N₂O₂Fe: 490.1343; found 490.1342. Anal. calcd for C₂₉H₂₆N₂O₂Fe: C, 71.03; H, 5.34. Found: C, 70.75; H, 5.53.

**(-)-2-[(2*R*_p-5,5-Diphenyl-ferrocenyl)](6*aS*,6*bS*)-6*b*,7,8,9-tetrahydro-5*H*-pyrrolo
[1',2':3,4]imidazo[5,1-*b*][1,3]oxazin-11(6*aH*)-one (*anti*-**199**).**

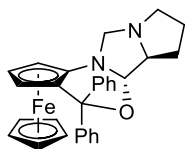


The following data were obtained for *anti*-**199**: mp 119-120 °C; $[\alpha]_D^{20}$ -230 (*c* 2.0, CHCl₃); CSP HPLC analysis (Chiralcel OD-H; eluent: 90:10 hexanes/*i*-PrOH, 1.0 mL/min) determined >99:1 er, >98% ee [*t*_R(major)

= 6.13 min, *t*_R(minor) = 9.88 min]; IR (KBr) ν_{\max} 3085, 3058, 3006, 2970, 2920, 1714, 1489, 1392, 1329 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.57 (d, 2H, *J* = 7.5 Hz), 7.40 (t, 2H, *J* = 7.2 Hz), 7.32-7.28 (m, 1H), 7.23-7.19 (m, 3H), 7.17-7.14 (m, 2H), 4.60 (d, 1H, *J*

= 1.5 Hz), 4.59-4.57 (m, 1H), 4.11 (t, 1H, $J = 8.4$ Hz), 4.07 (t, 1H, $J = 2.7$ Hz), 3.97-3.92 (m, 1H), 3.84 (s, 5H), 3.66-3.58 (m, 1H), 3.25-3.16 (m, 1H), 2.05-1.86 (m, 3H), 1.26 (m, 1H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 160.5, 145.9, 145.1, 128.4, 127.9, 127.8, 127.7, 126.8, 125.7, 93.1, 82.5, 82.3, 81.5, 69.9, 63.7, 62.8, 57.2, 46.3, 45.4, 28.7, 25.6; EIMS [m/z (%)] 490 (M^+ , 83), 86 (65), 84 (96), 51 (44), 49 (100), 47 (20), 47 (18); HRMS (EI) calcd for $\text{C}_{29}\text{H}_{26}\text{N}_2\text{O}_2^{56}\text{Fe}$: 490.1343; found 490.1348.

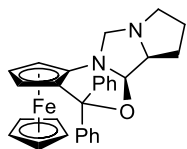
(–)-2-[(2*R*_p-5,5-Diphenyl-ferrocenyl)](6*aS*,6*bS*)6*a*,6*b*,7,8,9,11-hexahydro-5H-pyrrolo [1',2':3,4]imidazo[5,1-*b*][1,3]oxazine (*anti*-200**).**



To a solution of *anti*-**199** (195 mg, 0.40 mmol) in THF (20 mL) at -78 °C was added DIBAL-H (1.80 mL, 1.00 M solution in hexanes, 1.60 mmol). The reaction mixture was allowed to warm to room temperature overnight. After 16h, the solution was cooled to 0 °C and quenched with sat. aq. potassium sodium tartrate. It was then stirred for 15 min. to separate aqueous and organic layers. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 50:45:5 EtOAc/hexanes/ Et_3N , $R_f = 0.40$) afforded *anti*-**200** (114 mg, 0.24 mmol, 60%); mp 88-90 °C; $[\alpha]_{\text{D}}^{20} -343$ (c 1.0, CHCl_3); IR (KBr) ν_{max} 3084, 3026, 2954, 2919, 2865, 1491, 1473 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.51 (d, 2H, $J = 7.5$ Hz), 7.37 (t, 2H, $J = 7.2$ Hz), 7.28-7.23 (m, 6H), 4.32 (d, 1H, $J = 7.5$ Hz), 4.21 (d, 1H, $J = 7.5$ Hz), 4.12-4.11 (m, 1H), 4.06 (t, 1H, $J = 2.7$ Hz), 3.98 (d, 1H, $J = 2.7$ Hz), 3.87-3.82 (m, 1H), 3.80-3.79 (m, 1H), 3.77 (s, 5H), 3.20-3.13 (m, 1H), 2.72-2.64 (m, 1H), 2.15-2.07 (m, 1H), 1.79-1.68 (m, 2H), 1.61-1.55 (m, 1H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 146.7, 145.5, 128.1, 127.8, 127.6, 127.3, 126.4, 125.6, 102.6, 88.7, 84.2, 81.0,

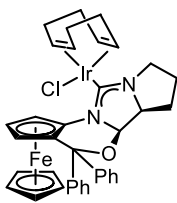
78.6, 70.2, 68.8, 63.0, 62.3, 54.9, 54.0, 29.4, 25.7; EIMS [*m/z* (%)] 476 (M^+ , 84), 83 (100), 56 (76), 57 (46), 41 (40); HRMS (EI) calcd for $C_{29}H_{28}N_2O^{56}Fe$: 476.1551; found 476.1544.

(–)-2-[(2*R*_p-5,5-Diphenyl-ferrocenyl)](6*aR*,6*bS*)6*a*,6*b*,7,8,9,11-hexahydro-5H-pyrrolo[1',2':3,4]imidazo[5,1-*b*][1,3]oxazine (*syn*-200**).**



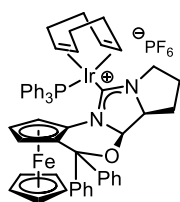
To a solution of *syn*-**199** (150 mg, 0.31 mmol) in THF (15 mL) at -78 °C was added DIBAL-H (1.40 mL, 1.00 M solution in hexanes, 1.60 mmol). The reaction mixture was allowed to warm to room temperature overnight. After 16 h, the solution was cooled to 0 °C and quenched with sat. aq. potassium sodium tartrate. It was then stirred for 15 min. to separate aqueous and organic layers. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 50:45:5 EtOAc/hexanes/ Et_3N , R_f = 0.23) afforded *syn*-**200** (115 mg, 0.24 mmol, 78%); mp 56-57 °C; $[\alpha]_D^{20}$ -318 (c 1.5, $CHCl_3$); IR (KBr) ν_{max} 3085, 3056, 2954, 2917, 2867, 1508, 1490, 1473 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, 2H, J = 7.5 Hz), 7.48 (t, 2H, J = 7.2 Hz), 7.40-7.37 (m, 1H), 7.14-7.12 (m, 3H), 6.99-6.96 (m, 2H), 5.07 (d, 1H, J = 4.5 Hz), 4.33 (s, 1H), 4.19 (d, 1H, J = 4.8 Hz), 4.04-3.99 (m, 2H), 3.89-3.88 (m, 1H), 3.72 (s, 5H), 3.56 (d, 1H, J = 4.8 Hz), 3.05-3.00 (m, 1H), 2.58-2.54 (m, 1H), 2.30-2.26 (m, 1H), 1.87-1.76 (m, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 147.7, 146.1, 127.6, 127.5, 127.5, 127.0, 126.9, 126.4, 102.9, 86.3, 81.9, 81.7, 77.4, 74.7, 69.6, 67.0, 63.7, 63.0, 59.6, 55.2, 26.9, 24.5; EIMS [*m/z* (%)] 476 (M^+ , 78), 83 (100), 56 (63), 41 (34), 43 (31); HRMS (EI) calcd for $C_{29}H_{28}N_2O^{56}Fe$: 476.1551; found 476.1547.

(-)-Chloro[η^4 -1,5-cyclooctadiene][(-)-2-[(2*R*_p-5,5-diphenyl-ferrocenyl)](6*aR*,6*bS*)-6*a*,6*b*,7,8,9,11-hexahydro-5*H*-pyrrolo[1',2':3,4]imidazol-2-ylidene]iridium (201**).**



A solution of *syn*-**200** (60.0 mg, 0.13 mmol) and tritylium tetrafluoroborate (42.0 mg, 0.13 mmol) in CH₂Cl₂ (2 mL) was stirred in a Schlenk flask at room temperature covered from light. After 5 h, solvent was removed *in vacuo* and the crude solid was washed with diethyl ether (3 x 5 mL) and dried *in vacuo*. To this was added Ir(μ -Cl)(cod)]₂ (42.0 mg, 0.06 mmol) and degassed THF (4 mL) in glovebox. The solution was cooled to -78 °C and with increased flow of argon, KO^tBu (14.0 mg, 0.13 mmol) was added at -78 °C. The reaction mixture was allowed to warm to room temperature. After 16 h, the volatiles were removed under reduced pressure and purification of the residue by flash column chromatography (silica gel, 2:8 EtOAc/hexanes) afforded **201** (26 mg, 0.03 mmol, 25%) as orange crystalline solid; *R*_f = 0.40 (3:7 EtOAc/hexanes); mp 157-158 °C; [α]_D²⁰ -49 (*c* 0.5, CHCl₃); IR (KBr) ν_{max} 3132, 2954, 2924, 2873, 1734, 1519, 1400 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.76 (d, 2H, *J* = 7.5 Hz), 7.53 (t, 2H, *J* = 7.2 Hz), 7.45 (t, 1H, *J* = 7.2 Hz), 7.12-7.10 (m, 3H), 6.95-6.92 (m, 2H), 6.13 (s, 1H), 5.69 (d, 1H, *J* = 7.8 Hz), 4.80-4.75 (m, 1H), 4.68-4.61 (m, 1H), 4.57-4.52 (m, 1H), 4.21-4.13 (m, 2H), 3.80-3.75 (s, 6H), 3.55-3.51 (m, 1H), 3.28-3.26 (m, 1H), 3.08-3.06 (m, 1H), 2.45-2.33 (m, 3H), 2.20-2.13 (m, 2H), 2.03-1.98 (m, 3H), 1.89-1.81 (m, 2H), 1.74-1.68 (m, 2H); ¹³C NMR (75.5 MHz, CDCl₃) δ 206.8, 146.6, 143.9, 128.2, 127.9, 127.7, 127.6, 127.5, 126.9, 94.4, 86.9, 86.6, 84.9, 83.1, 82.7, 70.2, 65.9, 65.0, 64.6, 61.7, 54.9, 49.6, 48.3, 34.7, 32.5, 30.4, 28.4, 25.9, 23.9; FABMS [*m/z* (%)] 810 (M⁺, 2), 95 (50), 91 (36), 67 (70), 55 (100), 43 (99), 39 (54), 29 (73); HRMS (FAB) calcd for C₃₇H₃₈N₂OCl⁵⁶FeIr: 810.1651; found 810.1613.

(-)-[η^4 -1,5-Cyclooctadiene][triphenylphosphine][2-[(2*R*_p-5,5-diphenyl ferrocenyl] - (6*aR*,6*bS*)6*a*,6*b*,7,8,9,11-hexahydro-5*H*-pyrrolo[1',2':3,4]imidazol-2-ylidene]iridium hexafluorophosphate (**202**).

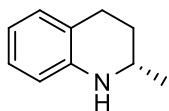


To a solution of **201** (13.0 mg, 0.02 mmol) in CH₂Cl₂ (0.5 mL) was added a solution of triphenylphosphine (4.00 mg, 0.02 mmol) in CH₂Cl₂ (0.5 mL) and resulting red solution was stirred for 3 h at room temperature and then concentrated. The residue was dissolved in minimum amount of CH₃CN and KPF₆ (3.50 mg, 0.02 mmol) in CH₃CN was added and stirred at room temperature for another hour, passed through Celite and washed with CH₂Cl₂. Volatiles were removed under reduced pressure and resulting red solid was triturated with pentane to afford **202** as red crystalline solid (17 mg, 0.02 mmol, 90%). mp 138-140 °C; [α]_D²⁰ – 319 (*c* 0.4, CHCl₃); IR (KBr) ν_{max} 3061, 2929, 2887, 1493, 1436, 1096, 847 cm⁻¹; ¹H NMR (300 MHz, acetone-*d*₆) δ 7.68-7.58 (m, 2H), 7.56-7.49 (m, 3H), 7.46-7.39 (m, 4H), 7.37-7.29 (m, 6H), 7.26-7.14 (m, 5H), 7.04 (t, 1H, *J* = 7.2 Hz), 6.87 (t, 2H, *J* = 7.8 Hz), 6.57 (d, 2H, *J* = 7.5 Hz), 6.16 (d, 1H, *J* = 7.8 Hz), 5.85-5.84 (m, 1H), 4.87-4.86 (m, 1H), 4.66-4.53 (m, 3H), 4.51-4.45 (m, 1H), 4.37-4.36 (m, 1H), 3.80 (s, 5H), 3.59-3.47 (m, 1H), 3.40-3.36 (m, 1H), 3.00-2.93 (m, 2H), 2.80-2.78 (m, 3H), 2.62-2.50 (m, 4H), 1.95-1.75 (m, 3H), 1.70 (m, 1H), 1.58-1.51 (m, 1H); ³¹P NMR (242.9 MHz, CDCl₃) 18.9 (s), – 144.3 (septet, *J* = 714.1 Hz); ¹⁹F NMR (564.7 MHz, CDCl₃) –73.6 (d, *J* = 711.6 Hz); ¹³C NMR (150.9 MHz, CDCl₃) δ 198.3 (d, *J* = 7.5 Hz), 146.9, 146.0, 134.0 (d, *J* = 12.1 Hz), 131.5 (d, *J* = 15.1 Hz), 128.6 (t, *J* = 10.6 Hz), 128.3, 127.9, 127.8, 127.7, 127.6, 95.2, 92.2, 85.6, 85.0, 84.1 (d, *J* = 13.6 Hz), 83.6, 80.2, 79.8, 70.8, 67.2, 65.7, 63.8, 63.1, 45.0,

35.1, 34.7, 28.1, 27.2, 25.7, 21.2. FABMS [m/z (%)] 1037 (M^+ , 17), 81 (42), 67 (41), 55 (100), 43 (93); HRMS (FAB) calcd for $C_{55}H_{53}N_2OP^{56}FeIr$: 1037.2874; found 1037.2682.

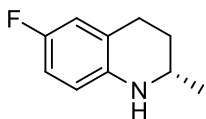
Hydrogenation of quinolines:

(S)-2-methyl-1,2,3,4-tetrahydroquinoline (203a).^{87, 90}



A solution of 2-methyl quinoline (0.07 mL, 0.51 mmol), triphenyl phosphine (1.31 mg, 1 mol%) and iridium catalyst **198** (6.00 mg, 1 mol%) in toluene (2 mL) in a vial was sealed in an autoclave. The autoclave was evacuated and back-filled with hydrogen three times, pressurized to 5 atm, and the mixture was stirred for 6 h at room temperature. The solvent was removed under reduced pressure and the crude reaction mixture was passed through a plug of silica gel, eluting with 2:94:4 EtOAc/hexanes/ Et_3N to give **203a** (69 mg, 0.39 mmol, 94 %) as colorless oil. $[\alpha]_D^{20} -53$ (c 3.0, $CHCl_3$) [lit^{83b} (*R*)- **203a** : $[\alpha]_D^{20} +84$ (c 0.2, $CHCl_3$, 99% ee)]. CSP HPLC analysis (Chiralcel OD-H; eluent: 98:2 hexanes/*i*-PrOH, 0.5 mL/min) determined 79:21 er, 58% ee [t_R (minor) = 14.16 min, t_R (major) = 16.17 min]; 1H NMR (300 MHz, $CDCl_3$) δ 7.01-6.97 (m, 2H), 6.63 (t, 1H, J = 7.6 Hz), 6.51-6.48 (m, 1H), 3.45-3.39 (m, 1H), 2.90-2.71 (m, 2H), 1.99-1.91 (m, 1H), 1.68-1.55 (m, 1H), 1.23 (d, 3H, J = 6.3 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 144.7, 129.2, 126.6, 121.0, 116.9, 113.9, 47.1, 30.0, 26.5, 22.5.

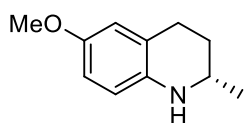
(S)-6-Fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (203b).^{87, 90}



A solution of 6-fluoro-2-methyl quinoline (80.6 mg, 0.51 mmol), triphenyl phosphine (1.31 mg, 1 mol%) and iridium catalyst **198** (6.00 mg, 1 mol%) in toluene (2 mL) in a vial was sealed in an autoclave. The autoclave was evacuated and back-filled with hydrogen three times, pressurized to 5 atm, and the

mixture was stirred for 10 h at room temperature. The solvent was removed under reduced pressure and the crude reaction mixture was passed through a plug of silica gel, eluting with 2:94:4 EtOAc/hexanes/Et₃N to give **203b** (77 mg, 0.47 mmol, 93%) as a white solid. $[\alpha]_D^{20} -77$ (c 0.6, CHCl₃) [lit^{83b} (R)- **203b** : $[\alpha]_D^{20} +80$ (c 0.2, CHCl₃, 98% ee)]; CSP HPLC analysis (Chiralcel OD-H; eluent: 98:2 hexanes/*i*-PrOH, 0.5 mL/min) determined 90:10 er, 80% ee [t_R (minor) = 12.55 min, t_R (major) = 16.66 min]; ¹H NMR (300 MHz, CDCl₃) δ 6.71-6.65 (m, 2H), 6.43-6.38 (m, 1H), 3.40-3.32 (bm, 2H), 2.83-2.67 (m, 2H), 1.95-1.88 (m, 1H), 1.63-1.50 (m, 1H), 1.21 (d, 3H, *J* = 6.3 Hz); ¹³C NMR (75.5 MHz, CDCl₃) δ 157.0, 153.9, 140.9, 122.5, 122.4, 115.5, 115.2, 114.7, 114.6, 113.3, 113.0, 47.3, 29.8, 26.7, 22.4.

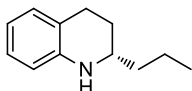
(S)-6-Methoxy-2-methyl-1,2,3,4-tetrahydroquinoline (203c).^{83b, 87, 90}



A solution of 6-methoxy-2-methyl quinoline (86.6 mg, 0.50 mmol), triphenyl phosphine (1.31 mg, 1 mol%) and iridium catalyst **198** (6.00 mg, 1 mol%) in toluene (2 mL) in a vial was sealed in an autoclave. The autoclave was evacuated and back-filled with hydrogen three times, pressurized to 5 atm, and the mixture was stirred for 24 h at room temperature. The solvent was removed under reduced pressure and the crude reaction mixture was passed through a plug of silica gel, eluting with 10:86:4 EtOAc/hexanes/Et₃N to give **203c** (69 mg, 0.39 mmol, 78%) as an yellow oil, which solidifies on standing. $[\alpha]_D^{20} -60$ (c 1.0, CHCl₃) [lit^{83b} (R)- **203c** : $[\alpha]_D^{20} +80$ (c 0.19, CHCl₃, >99% ee)]; CSP HPLC analysis (Chiralcel OD-H; eluent: 98:2 hexanes/*i*-PrOH, 0.5 mL/min) determined 79:21 er, 58% ee [t_R (minor) = 19.58 min, t_R (major) = 22.85 min]; ¹H NMR (300 MHz, CDCl₃) δ 6.62-6.58 (m, 2H), 6.47-6.44 (m, 1H, *J* = 8.1Hz), 3.73 (s, 3H), 3.33 (bs, 1H), 2.85-2.69 (m, 2H), 1.96-1.88 (m, 1H), 1.65-

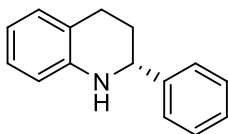
1.51 (m, 1H), 1.22-1.20 (d, 3H, $J = 6.3$ Hz); ^{13}C NMR (75.5 MHz, CDCl_3) δ 151.8, 138.8, 122.5, 115.5, 114.6, 112.8, 55.8, 47.4, 30.3, 26.9, 22.5.

(S)-2-Propyl-1,2,3,4-tetrahydroquinoline (203d).^{87,90}



A solution of 2-propyl quinoline (0.08 mL, 0.50 mmol), triphenyl phosphine (1.31 mg, 1 mol%) and iridium catalyst **198** (6.00 mg, 1 mol%) in toluene (2 mL) in a vial was sealed in an autoclave. The autoclave was evacuated and back-filled with hydrogen three times, pressurized to 5 atm, and the mixture was stirred for 24 h at room temperature. The solvent was removed under reduced pressure and the crude reaction mixture was passed through a plug of silica gel, eluting with 2:94:4 EtOAc/hexanes/ Et_3N to give **203d** (68 mg, 0.39 mmol, 78%) as colorless oil. $[\alpha]_{\text{D}}^{20} -48$ (c 1.1, CHCl_3) [lit^{83b} (*R*)-**203d**: $[\alpha]_{\text{D}}^{20} +80$ (c 0.2, CHCl_3 , 99% ee)]. CSP HPLC analysis (Chiralcel OD-H; eluent: 98:2 hexanes/*i*-PrOH, 0.5 mL/min) determined 69:31 er, 38% ee [$t_{\text{R}}(\text{minor}) = 12.46$ min, $t_{\text{R}}(\text{major}) = 14.84$ min]; ^1H NMR (300 MHz, CDCl_3) δ 6.98 (t, 2H, $J = 6.6$ Hz), 6.61 (t, 1H, $J = 7.8$ Hz), 6.50 (d, 1H, $J = 8.1$ Hz), 3.80 (bs, 1H) 3.29-3.25 (m, 1H), 2.84-2.75 (m, 2H), 2.01-1.95 (m, 1H), 1.66-1.59 (m, 1H), 1.54-1.42 (m, 4H), 0.98 (t, 3H, $J = 6.9$ Hz); ^{13}C NMR (75.5 MHz, CDCl_3) δ 144.6, 129.2, 126.6, 121.4, 116.9, 114.0, 51.3, 38.8, 28.1, 26.4, 18.9, 14.2.

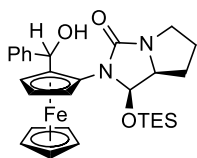
(R)-2-Phenyl-1,2,3,4-tetrahydroquinoline (203e).^{83b, 87, 90, 135}



A solution of 2-phenyl quinoline (103 mg, 0.50 mmol), triphenyl phosphine (1.31 mg, 1 mol%) and iridium catalyst **198** (6.00 mg, 1 mol%) in toluene (2 mL) in a vial was sealed in an autoclave. The autoclave was evacuated and back-filled with hydrogen three times, pressurized to 5 atm, and the mixture was stirred for 24 h at room temperature. The solvent was removed under

reduced pressure and the product was separated by using preparative TLC, with 5:95 EtOAc/hexanes to give **203e** (26 mg, 0.12 mmol, 25%) as an yellow solid. $[\alpha]_D^{20} +18$ (*c* 0.4, CHCl₃) [lit¹³⁶ (*R*)- **203e** : $[\alpha]_D^{20} +42$ (*c* 1.0, CHCl₃, 98% ee)]; CSP HPLC analysis (Chiralcel OD-H; eluent: 95:5 hexanes/*i*-PrOH, 0.6 mL/min) determined 75:25 er, 50% ee [*t*_R(minor) = 17.68 min, *t*_R(major) = 22.35 min]; ¹H NMR (300 MHz, CDCl₃) δ 7.42-7.27 (m, 5H), 7.01 (t, 2H, *J* = 6.9 Hz), 6.65 (t, 1H, *J* = 7.5 Hz), 6.54 (d, 1H, *J* = 8.1 Hz), 4.45 (dd, 1H, *J* = 9.3, 3.3 Hz), 4.07 (bs, 1H), 2.99-2.90 (m, 1H), 2.74 (dt, 1H, *J* = 16.5, 4.8 Hz), 2.17-2.03 (m, 2H); ¹³C NMR (75.5 MHz, CDCl₃) δ 144.8, 144.7, 129.3, 128.5, 127.4, 126.9, 126.5, 120.8, 117.1, 113.9, 56.2, 30.9, 26.4.

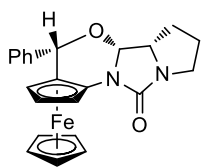
(+)-2-[2*S*_p-(Phenylhydroxymethyl)ferrocenyl]-1*R*-triethylsilyloxy-7*aS* hexahydropyrrolo[1,2-*c*]imidazol-3-one (188j**).**



A solution of *syn*-**187** (1.00 g, 2.27 mmol) in THF (26 mL) at -78°C was exposed to *t*-BuLi (4.99 mL, 1.00 M in pentane, 4.99 mmol). After stirring for 30 min, a distinct colour change from orange to orange-red was observed. The solution was quenched with benzaldehyde (0.58 mL, 5.68 mmol) and stirred for 2 h. Workup was conducted by addition of water (0.5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether (2×40 mL). The combined organic extract was washed with water, brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 0.8:9:0.2 EtOAc/hexanes/Et₃N, *R*_f = 0.06) afforded **188j** (696 mg, 1.27 mmol, 56%) as yellow solid; mp 121-124 $^\circ\text{C}$; $[\alpha]_D^{20} = +112$ (*c* 1.0, acetone); IR (KBr) ν_{max} 3298, 2954, 2910, 2874, 1680, 1476, 1413, 1286, 1242, 1088, 1001 cm⁻¹; ¹H NMR (300MHz, acetone-*d*₆) δ 7.45 (d, 2H, *J* = 8.4 Hz), 7.36 (t, 2H, *J* = 8.1 Hz), 7.25 (t,

1H, $J = 7.2$ Hz), 5.88 (d, 1H, $J = 1.5$ Hz), 5.63 (d, 1H, $J = 6.9$ Hz), 5.39 (s, 1H), 4.56 (t, 1H, $J = 2.4$ Hz), 4.42 (s, 5H), 4.14-4.07 (m, 1H), 3.98 (t, 1H, $J = 2.4$ Hz), 3.65-3.59 (m, 2H), 3.19-3.11 (m, 1H), 2.01-1.99 (m, 3H), 1.85-1.81 (m, 1H), 0.85 (t, 9H, $J = 7.8$ Hz), 0.49 (dq, 6H, $J = 7.8, 2.0$ Hz); ^{13}C NMR (75.5 MHz, acetone- d_6) δ 161.3, 145.7, 128.9, 128.0, 93.4, 91.8, 85.6, 70.9, 69.2, 68.8, 68.6, 64.2, 63.1, 47.6, 27.4, 26.4, 7.6, 5.8; EIMS [m/z (%)] 546 (M^+ , 1.3), 414 (25), 243 (13), 150 (22), 135 (100), 121 (17), 107 (48), 103 (64); HRMS (EI) calcd for $\text{C}_{29}\text{H}_{38}\text{N}_2\text{O}_3\text{Si}^{56}\text{Fe}$: 546.2001; found 546.1998. Anal. calcd for $\text{C}_{29}\text{H}_{38}\text{N}_2\text{O}_3\text{Si}^{56}\text{Fe}$: C, 63.79; H, 7.01. Found: C, 64.18, H, 6.97.

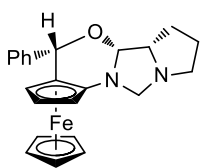
(+)-2-[2S_p-Ferrocenyl-(5S,6aR,6bS)-5-phenyl-6b,7,8,9-tetrahydro-5H-pyrrolo[1',2':3,4]imidazo[5,1-b][1,3]oxazin-11(6aH)-one (204).



To a solution of **188j** (695 mg, 1.27 mmol) in CHCl_3 (40 mL) at room temperature was added *p*-toluenesulfonic acid monohydrate (483 mg, 2.54 mmol). After stirring for 5 min, a distinct color change from orange to orange-brown was observed. The solution was quenched with saturated aqueous NaHCO_3 (15 mL). The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 1.3:8.5:0.2 EtOAc/hexanes/ Et_3N , $R_f = 0.35$) afforded **204** (265 mg, 0.64 mmol, 50%) as yellow solid; mp 160 °C; $[\alpha]_{\text{D}}^{20} = +80$ (c 1.0, CHCl_3); IR (KBr) ν_{max} 2971, 2867, 2726, 1702, 1462, 1452, 1377, 1215, 761 cm^{-1} ; ^1H NMR (600 MHz, acetone- d_6) δ 7.62 (d, 2H, $J = 7.2$ Hz), 7.49 (t, 2H, $J = 3.6$ Hz), 7.38 (t, 1H, $J = 3.6$ Hz), 5.77 (s, 1H), 5.40 (d, 1H, $J = 3.6$ Hz), 4.35 (s, 1H), 4.13 (q, 1H, $J = 3.9, 3.6$ Hz), 3.95 (s, 1H) 3.80 (s, 5H), 3.79 (s, 1H), 3.72-3.70 (m, 1H), 3.10-3.06 (m, 1H), 2.34-2.29 (m, 1H) 2.09-1.97 (m, 4H); ^{13}C NMR (150.9 MHz, acetone- d_6) δ 159.7, 140.1, 128.0,

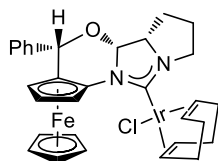
127.3, 125.5, 93.2, 83.4, 80.1, 75.7, 69.4, 63.0, 61.0, 60.7, 55.9, 45.8, 25.5, 24.8; EIMS [m/z (%)] 414 (M^+ , 100), 412 (11), 121 (16), 56 (13); HRMS (EI) calcd for $C_{23}H_{22}N_2O_2^{56}Fe$: 414.1030; found 414.1038. Anal. calcd for $C_{23}H_{22}N_2O_2^{56}Fe$: C, 66.68; H, 5.35. Found: C, 67.14, H, 5.60.

(+)-2-[2*S_p*-Ferrocenyl-(5*S*,6*aR*,6*bS*)-5-phenyl-6*b*,7,8,9-tetrahydro-5*H*-pyrrolo [1',2':3,4]imidazo[5,1-*b*][1,3]oxazine (205).



To a solution of **204** (260 mg, 0.63 mmol) in THF (30 mL) at $-78\text{ }^{\circ}\text{C}$ was added drop-wise a solution of DIBAL-H (2.51 mL, 1.00 M in hexanes, 2.51 mmol). The solution was left to warm up to room temperature for 18 h. The solution was cooled to $0\text{ }^{\circ}\text{C}$ and quenched with sat. aq. potassium sodium tartrate. It was then stirred for 15 min. to separate aqueous and organic layers. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 5:4.5:0.5 EtOAc/hexanes/ Et_3N , $R_f = 0.43$) afforded **205** (101 mg, 0.25 mmol, 40%) as yellow crystals; mp $165\text{ }^{\circ}\text{C}$; $[\alpha]_D^{20} = +104$ (c 0.9, acetone); IR (KBr) ν_{max} 2953, 2908, 2863, 2726, 1462, 1377, 1302, 724 cm^{-1} ; 1H NMR (300 MHz, acetone- d_6) δ 7.55 (d, 2H, $J = 7.5$ Hz), 7.48 (t, 2H, $J = 7.5$ Hz), 7.34 (t, 1H, $J = 7.5$ Hz), 5.55 (s, 1H), 4.63 (d, 1H, $J = 4.8$ Hz), 4.28 (d, 1H, $J = 6.0$ Hz), 4.17 (d, 1H, 5.7 Hz), 3.88 (t, 1H, $J = 2.7$ Hz), 3.81 (s, 6H), 3.73-3.67 (m, 1H), 3.61 (dd, 1H, $J = 2.4, 1.2$ Hz), 3.22-3.08 (m, 2H), 2.46-2.32 (m, 1H), 2.20-2.08 (m, 1H), 1.91-1.88 (m, 2H); ^{13}C NMR (75.5 MHz, acetone- d_6): δ 142.1, 128.5, 127.5, 126.0, 106.7, 90.6, 83.1, 77.4, 76.4, 69.2, 67.6, 62.9, 60.1, 54.4, 53.1, 26.4, 24.0; EIMS [m/z (%)] 400 (M^+ , 10), 205 (12), 79 (10), 59 (28), 43 (100); HRMS (EI) calcd for $C_{23}H_{24}N_2O^{56}Fe$: 400.1238; found 400.1235.

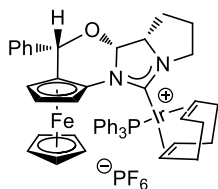
(-)-Chloro[η^4 -1,5-cyclooctadiene-2-[2*S_p*-Ferrocenyl-(5*S*,6*aR*,6*bS*)-5-phenyl-6*b*,7,8,9-tetrahydro-5*H*-pyrrolo[1',2':3,4]imidazol-2-ylidene]iridium (207).



A solution of **205** (100 mg, 0.24 mmol) and tritylium tetrafluoroborate (80.0 mg, 0.24 mmol) in CH_2Cl_2 (4 mL) was stirred in a Schlenk flask at room temperature covered from light. After 16 h, solvent was removed *in vacuo* and the crude solid was washed with dry diethyl ether (3×5 mL) and dried *in vacuo*. To this was added $\text{Ir}(\mu\text{-Cl})(\text{cod})_2$ (81.1 mg, 0.12 mmol) and degassed THF (8 mL) in glovebox. The solution was cooled to -78°C and with increased flow of argon, KO^tBu (27.0 mg, 0.24 mmol) was added at -78°C . The solution was allowed to warm up to room temperature and stirred for 16 h. The volatiles were removed under reduced pressure and purification of the residue by flash column chromatography (silica gel, 0.8:8.8:0.4 EtOAc/hexanes/ Et_3N , $R_f = 0.19$) afforded **207** (32 mg, 0.04 mmol, 36 %); mp 175°C (decomposition); $[\alpha]_{\text{D}}^{20} = -182$ (c 0.8, acetone); IR (KBr) ν_{max} 3020, 2928, 2857, 1507, 1420, 1216, 929, 758, 670 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.56 (d, 2H, $J = 7.2$ Hz), 7.47 (t, 2H, $J = 7.2$ Hz), 7.38 (t, 1H, $J = 6.9$ Hz), 5.90 (dd, 1H, $J = 2.4, 1.2$ Hz), 5.78 (s, 1H), 5.32 (d, 1H, $J = 8.1$ Hz), 4.96-4.91 (m, 2H), 4.57 (td, 1H, $J = 10.5, 5.1$ Hz), 4.06-4.04 (m, 5H), 3.91-3.90 (m, 2H), 3.45-3.41 (m, 1H), 3.23 (t, 1H, $J = 7.05$ Hz), 2.62 (dt, 1H, $J = 7.5, 3.6$ Hz), 2.52-2.37 (m, 4H), 2.35-1.86 (m, 4H), 1.77-1.47 (m, 5H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 210.7, 139.2, 128.2, 128.0, 127.8, 127.3, 125.3, 94.8, 90.2, 87.2, 86.5, 70.9, 64.7, 63.0, 61.1, 57.8, 56.7, 51.2, 49.3, 35.0, 31.9, 31.0, 29.7, 27.9, 24.6, 24.0; FABMS [m/z (%)] 732 (M^+ , 1.9), 243

(41), 220 (13), 211 (40), 205 (51), 183 (94); HRMS (FAB) calcd for $C_{31}H_{34}N_2O^{56}FeCl^{191}Ir$: 732.1318; found 732.1290.

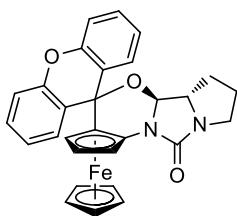
(-)-[η^4 -1,5-Cyclooctadiene][triphenylphosphine]{2-[2*S*_p-Ferrocenyl-(5*S*,6*aR*,6*bS*)-5-phenyl-6*b*,7,8,9-tetrahydro-5*H*-pyrrolo[1',2':3,4]imidazol-2-ylidene}iridium hexafluorophosphate (208**).**



To a solution of **207** (16.0 mg, 0.02 mmol) in CH_2Cl_2 (1 mL) was added a solution of triphenylphosphine (5.80 mg, 0.02 mmol) in CH_2Cl_2 (1 mL) and resulting red solution was stirred for 3 h at room temperature and then concentrated under reduced pressure. The residue was dissolved in minimum amount of CH_3CN and KPF_6 (4.80 mg, 0.03 mmol) in CH_3CN (1 mL) was added. Addition of a small amount CH_2Cl_2 (0.3 mL) was needed to achieve complete solvation. The solution was stirred at room temperature for another hour, passed through Celite and washed with CH_2Cl_2 . Volatiles were removed under reduced pressure and resulting red solid was triturated with pentane to afford **207** as red crystalline solid (16 mg, 0.02 mmol, 66%). mp 225-227 °C (dec.); $[\alpha]_D^{20} -100$ (*c* 0.8, $CHCl_3$); IR (KBr) ν_{max} 2955, 2860, 2726, 1733, 1462, 1377, 723 cm^{-1} ; 1H NMR (300 MHz, acetone- d_6) δ 7.77-7.70 (m, 15H), 7.57 (t, 3H, $J = 7.2$ Hz), 7.47-7.32 (m, 4H), 7.39 (t, 2H, $J = 6.3, 1.2$ Hz), 6.00 (s, 1H), 5.59 (d, 1H, $J = 9.3$ Hz), 5.25 (t, 1H, $J = 1.2$ Hz), 4.93-4.89 (m, 1H), 4.46-4.44 (m, 1H), 4.35 (t, 1H, $J = 2.4$ Hz), 4.31-4.26 (m, 1H), 4.23 (t, 1H, $J = 1.05$ Hz), 3.69 (t, 2H, $J = 7.8$ Hz), 3.52-3.48 (m, 1H), 3.35 (s, 5H), 2.75-2.70 (m, 2H), 2.56-2.43 (m, 1H), 2.35-2.27 (m, 2H), 2.02-1.95 (m, 5H), 1.87-1.79 (m, 3H); ^{31}P NMR (242.9 MHz, $CDCl_3$) 20.61 (s), -144.3 (septet, $J = 707.0$ Hz); ^{19}F NMR (282.4 MHz, $CDCl_3$) -73.6 (d, $J =$

711.6 Hz); FABMS [m/z (%)] 961 (M^+ , 0.9), 167 (20), 150 (17), 149 (100), 113 (19), 95 (14); HRMS (FAB) calcd for $C_{49}H_{49}N_2O^{56}FeP^{191}Ir$: 961.2561; found 961.2507.

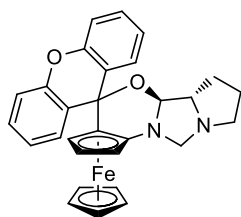
(-)-2-[2*S_p*-Ferrocenyl](6*aS*,6*bS*)6*b*,7,8,9 tetrahydrospiro[pyrrolo[1',2':3,4]imidazo[5,1-*b*][1,3]oxazine-5,9'-xanthen]-11(6*aH*)-one (209).



To a solution of *syn*-**187** (760 mg, 1.73 mmol) in THF (15 mL) at –78 °C was added *t*-BuLi (4.20 mL, 0.90 M in pentane, 3.80 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with a solution of xanthone (847 mg, 4.32 mmol) in THF (5 mL) and stirred for 30 min. at that temperature. On addition of xanthone, reaction mixture turned reddish-brown in color. Workup was conducted by addition of water (0.5 mL) and after warming to room temperature, the reaction mixture was extracted with diethyl ether (2 × 50 mL). The combined organic extract was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, R_f = 0.30) afforded a mixture of starting material and product which was taken to the next step. The mixture was dissolved in $CHCl_3$ and *p*-toluenesulfonic acid monohydrate (657 mg, 3.45 mmol) was added and stirred for 10 min.. The solution was quenched with saturated aqueous $NaHCO_3$ (10 mL). The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, R_f = 0.20) afforded **209** (444 mg, 0.88 mmol, 51% over two steps); mp >230 °C; $[\alpha]_D^{20}$ –14 (c 1.0, $CHCl_3$); IR (KBr) ν_{max} 3075, 3040, 2959, 2928, 2893, 1713,

1598, 1510, 1450, 1394, 1238, 1042 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.97 (dd, 1H, J = 7.5, 1.2 Hz), 7.46-7.28 (m, 4H), 7.20-7.08 (m, 2H), 6.98 (td, 1H, J = 7.8, 1.2 Hz), 6.21 (s, 1H), 4.98 (s, 1H), 4.03-3.97 (m, 1H), 3.90-3.86 (m, 6H), 3.78-3.69 (m, 1H), 3.55 (s, 1H), 3.28-3.22 (m, 1H), 2.34-2.25 (m, 1H), 2.20-2.11 (m, 1H), 2.08-1.98 (m, 1H), 1.76-1.62 (m, 1H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 158.7, 150.4, 149.5, 130.5, 128.8, 128.5, 128.3, 126.0, 125.1, 123.8, 122.9, 116.8, 116.3, 89.6, 85.7, 83.9, 72.3, 69.7, 64.4, 64.1, 62.0, 59.3, 45.5, 28.5, 25.8; EIMS [m/z (%)] 504 (M^+ , 100), 407 (16), 181 (47), 70 (15), 44 (16), 43 (49); HRMS (EI) calcd for $\text{C}_{29}\text{H}_{24}\text{N}_2\text{O}_3$ ^{56}Fe : 504.1136; found 504.1148. Anal. calcd for $\text{C}_{29}\text{H}_{24}\text{N}_2\text{O}_3$ ^{56}Fe : C, 69.06; H, 4.80. Found: C, 69.07, H, 4.85.

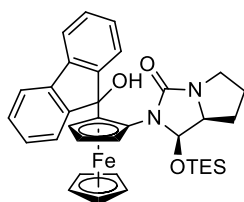
(-)-2-[2*S_p*-Ferrocenyl](6*aS*,6*bS*)-6*a*,6*b*,7,8,9,11-hexahydrospiro[pyrrolo[1',2':3,4]imidazo[5,1-*b*][1,3]oxazine-5,9'-xanthene (210).



To a solution of **209** (123 mg, 0.24 mmol) in THF (30 mL) at -78°C was added drop-wise a solution of DIBAL-H (1.10 mL, 1.00 M in hexanes, 2.51 mmol). The solution was left to warm up to room temperature for 20 h. The solution was cooled to 0°C and quenched with sat. aq. potassium sodium tartrate. It was then stirred for 15 min. to separate aqueous and organic layers. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 5:4.5:0.5 EtOAc/hexanes/ Et_3N , R_f = 0.15) afforded **210** (60 mg, 0.12 mmol, 50%) as an yellow solid; mp 220°C (dec.); $[\alpha]_{\text{D}}^{18} = +3$ (c 1.5, CHCl_3); IR (KBr) ν_{max} 3072, 2925, 2850, 1469, 1448, 1362, 1278 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.83 (d, 1H, J = 7.5 Hz), 7.51 (d, 1H, J = 7.5 Hz), 7.41-7.30 (m, 3H), 7.20-7.13 (m, 2H), 7.02-6.96 (m, 1H), 5.67 (s, 1H), 4.24 (s, 1H), 4.11 (d, 1H, J = 6.9 Hz), 4.04-3.99

(m, 1H, $J = 6.6$ Hz), 3.86 (d, 1H, $J = 7.2$ Hz), 3.78 (s, 5H), 3.73-3.72 (m, 2H), 3.32-3.26 (m, 1H), 2.95-2.88 (m, 1H), 2.40-2.34 (m, 1H), 2.04-1.81 (m, 3H); ^{13}C NMR (75.5 MHz, CDCl_3): δ 150.9, 150.6, 132.0, 131.2, 128.2, 127.8, 125.0, 124.1, 123.5, 123.0, 116.7, 116.5, 97.4, 93.8, 84.1, 75.5, 71.5, 70.8, 69.5, 63.4, 62.1, 59.2, 56.2, 30.6, 26.8; EIMS [m/z (%)] 490 (M^+ , 14), 86 (61), 84 (100), 71 (23), 69 (19), 55 (27); HRMS (EI) calcd for $\text{C}_{29}\text{H}_{26}\text{N}_2\text{O}_2^{56}\text{Fe}$: 490.1343; found 490.1345. Anal. calcd for $\text{C}_{29}\text{H}_{26}\text{N}_2\text{O}_2^{56}\text{Fe}$: C, 71.03; H, 5.34. Found: C, 71.01, H, 5.59.

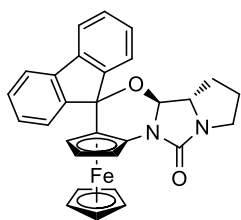
(-)-2-[2*S*_p-(9-Hydroxy-9H-fluoren-9-yl)ferrocenyl]-1*R*-triethylsilyloxy-7*aS*-hexahydropyrrolo[1,2-*c*]imidazol-3-one (188k).



To a solution of *syn*-**187** (2.00 g, 4.54 mmol) in THF (40 mL) at -78°C was added *t*-BuLi (10.0 mL, 1.00 M in pentane, 9.99 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with a solution of fluorenone (2.03 g, 11.2 mmol) in THF (30 mL) and stirred for 30 min. at that temperature. Workup was conducted by addition of water (1.0 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether (2×50 mL). The combined organic extract was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.27$) afforded **188k** (2.04 g, 3.30 mmol, 71%) as a diastereomerically enriched orange solid; mp $205\text{--}206^\circ\text{C}$; $[\alpha]_{\text{D}}^{18} +53$ (c 1.0, CHCl_3); IR (neat) ν_{max} 3165, 2953, 2909, 2875, 1673, 1459, 1097, 1001 cm^{-1} ; ^1H NMR (300 MHz, acetone- d_6) δ 8.03 (s, 1H), 7.99-7.96 (m, 1H), 7.68-7.63 (m, 2H), 7.51 (d, 1H, $J = 7.5$ Hz), 7.45-7.37 (m, 2H), 7.17 (t, 1H, $J = 7.2$ Hz), 7.07 (t, 1H, $J = 7.5$ Hz), 5.89 (d, 1H, $J =$

7.2 Hz), 4.78 (t, 1H, $J = 1.8$ Hz), 4.47 (m, 5H), 4.10-4.07 (m, 1H), 3.91 (t, 1H, $J = 2.7$ Hz), 3.80-3.74 (m, 1H), 3.25-3.18 (m, 2H), 2.14-2.09 (m, 2H), 2.01-1.95 (m, 2H), 0.65 (t, 9H, $J = 7.8$ Hz), 0.47-0.39 (m, 6H); ^{13}C NMR (75.5 MHz, acetone- d_6) δ 162.1, 153.7, 152.2, 140.6, 138.8, 129.3, 128.4, 127.8, 127.7, 126.5, 126.4, 120.4, 119.9, 91.5, 88.8, 84.3, 81.0, 70.9, 69.5, 68.7, 64.0, 63.2, 47.6, 26.4, 26.0, 6.83, 5.06; EIMS [m/z (%)] 498 (M^+ , 5), 236 (20), 221 (35), 198 (11), 281 (28), 180 (100); HRMS (EI) calcd for $\text{C}_{35}\text{H}_{40}\text{N}_2\text{O}_3\text{Si}^{56}\text{Fe}$: 620.2157; found 620.2149. Anal. calcd for $\text{C}_{35}\text{H}_{40}\text{N}_2\text{O}_3\text{Si}^{56}\text{Fe}$: C, 67.73; H, 6.50. Found: C, 68.00, H, 6.63.

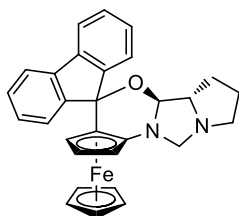
(–)-2-[2*S_p*-Ferrocenyl](6*aS*,6*bS*)6*b*,7,8,9-tetrahydrospiro[pyrrolo[1',2':3,4]imidazo[5,1-*b*][1,3]oxazine-5,9'-fluoren]-11(6*aH*)-one (211).



To a solution of **188k** (800 mg, 1.29 mmol) in CHCl_3 (20 mL) at room temperature was added *p*-toluenesulfonic acid monohydrate (981 mg, 5.16 mmol). After stirring for 5 min, a distinct color change from orange to orange-brown was observed. The solution was quenched with saturated aqueous NaHCO_3 (10 mL). The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.14$) afforded **211** (402 mg, 0.82 mmol, 64%), as a yellow solid; mp 210-212 °C; $[\alpha]_D^{18} = -15$ (c 1.0, CHCl_3); IR (neat) ν_{max} 3092, 2944, 2928, 2894, 2873, 1698, 1496, 1448, 1392, 1106, 1027 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.14 (d, 1H, $J = 3.6$ Hz), 7.68-7.66 (m, 1H), 7.54-7.45 (m, 3H), 7.27-7.23 (m, 1H), 7.10 (t, 1H, $J = 7.5$ Hz), 6.85 (d, 1H, $J = 7.5$ Hz), 6.07 (s, 1H), 5.22 (s, 1H), 4.22 (s, 5H), 3.98 (s, 1H), 3.73-3.65 (m, 2H), 3.22-3.14 (m, 2H), 2.13-1.95 (m, 2H), 1.93-1.89 (m, 1H), 1.66-1.62 (m, 1H); ^{13}C

NMR (75.5 MHz, CDCl₃) δ 158.7, 150.2, 148.1, 140.6, 137.7, 129.6, 129.0, 128.6, 127.2, 125.9, 124.4, 120.2, 119.4, 92.5, 84.3, 83.8, 69.8, 63.9, 63.8, 60.9, 60.0, 45.3, 28.4, 25.7; EIMS [*m/z* (%)] 488 (*M*⁺, 75), 362 (14), 70 (15), 61 (15), 45 (15), 43 (100); HRMS (EI) calcd for C₂₉H₂₄N₂O₂⁵⁶Fe: 488.1187; found 488.1177.

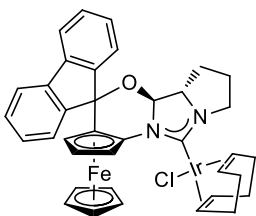
(+)-2-[2*S_p*-Ferrocenyl](6*aS*,6*bS*)6*a*,6*b*,7,8,9,11-hexahydrospiro[pyrrolo[1',2':3,4]imidazo[5,1-*b*][1,3]oxazine-5,9'-fluorene (212**).**



To a solution of **211** (402 mg, 0.82 mmol) in THF (30 mL) at –78 °C was added drop-wise a solution of DIBAL-H (3.60 mL, 0.90 M in hexanes, 3.29 mmol). The solution was left to warm up to room temperature for 20 h. The solution was cooled to 0 °C and quenched with sat. aq. potassium sodium tartrate. It was then stirred for 15 min. to separate aqueous and organic layers. The organic layer was washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 5:4.5:0.5 EtOAc/hexanes/Et₃N, *R_f* = 0.20) afforded **212** (96 mg, 0.20 mmol, 25%) as a yellow solid; mp 215-216 °C; [α]_D¹⁸ = +94 (*c* 0.5, CHCl₃); IR (neat) ν_{max} 3080, 3022, 2922, 2870, 1497, 1447, 1151, 1028, 730 cm^{–1}; ¹H NMR (300 MHz, CDCl₃) δ 8.14 (t, 1H, *J* = 4.8 Hz), 7.69-7.66 (m, 1H), 7.55 (d, 1H, *J* = 7.2 Hz), 7.46-7.43 (m, 2H), 7.30-7.25 (m, 1H), 7.12 (t, 1H, *J* = 7.2 Hz), 6.92 (d, 1H, *J* = 7.5 Hz), 5.49 (s, 1H), 4.44 (s, 1H), 4.17 (s, 5H), 4.04 (q, 2H, *J* = 6.9 Hz), 3.87 (s, 1H), 3.65-3.63 (m, 1H), 3.25 (s, 2H), 2.95-2.93 (m, 1H), 2.23-2.21 (m, 1H), 1.99-1.83 (m, 3H); ¹³C NMR (75.5 MHz, CDCl₃): δ 150.9, 149.5, 140.4, 138.3, 129.1, 128.8, 128.2, 127.0, 126.1, 124.4, 120.0, 119.3, 101.0, 91.5, 83.5, 77.2, 76.7, 75.2, 70.5, 69.6, 62.9, 61.3, 59.8,

55.8, 30.4, 26.5; EIMS [m/z (%)] 474 (M^+ , 84), 391 (16), 362 (14), 84 (24), 83 (100), 56 (23); HRMS (EI) calcd for $C_{29}H_{26}N_2O^{56}Fe$: 474.1394; found 474.1382.

(-)-Chloro[η^4 -1,5-cyclooctadiene[(-)-2-[2*S*_p-ferrocenyl-(6*aS*,6*bS*)6*a*,6*b*,7,8,9,11-hexahydrospiropyrrolo[1',2':3,4]imidazo[5,1-*b*][1,3]oxazine-5,9'-fluorene]ylidene]iridium (214**).**

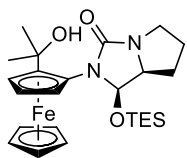


A solution of **212** (45.0 mg, 0.09 mmol) and tritylium tetrafluoroborate (31.0 mg, 0.09 mmol) in CH_2Cl_2 (2 mL) was stirred in a Schlenk flask at room temperature covered from light.

After 16 h, solvent was removed *in vacuo* and the crude solid was washed with dry diethyl ether (3×5 mL) and dried *in vacuo*. To this was added $Ir(\mu-Cl)(cod)_2$ (32.0 mg, 0.05 mmol) and degassed THF (3 mL) in glovebox. The solution was cooled to -78 °C and with increased flow of argon, $KOtBu$ (10.0 mg, 0.24 mmol) was added at -78 °C. The solution was allowed to warm up to room temperature and stirred for 16 h. The volatiles were removed under reduced pressure and purification of the residue by flash column chromatography (silica gel, 2:8 EtOAc/hexanes, $R_f = 0.20$) afforded **214** (21 mg, 0.02 mmol, 27 %). $[\alpha]_D^{18} = -6$ (c 1.2, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2981, 2926, 2876, 2853, 2838, 1518, 1448, 1428, 1215, 972, 913 cm^{-1} ; 1H NMR (600 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.66 (d, 1H, $J = 6.6$ Hz), 7.54 (d, 1H, $J = 7.2$ Hz), 7.50-7.45 (m, 3H), 7.10 (t, 1H, $J = 7.8$ Hz), 6.71 (d, 1H, $J = 7.2$ Hz), 6.39 (d, 1H, $J = 3.0$ Hz), 6.26 (s, 1H), 4.85 (m, 1H), 4.71-4.70 (m, 1H), 4.52-4.48 (m, 1H), 4.34 (s, 5H), 4.05 (s, 1H), 3.87 (m, 1H), 3.54 (m, 1H), 3.32-3.26 (m, 2H), 2.93 (m, 1H), 2.37-2.15 (m, 7H), 2.01-1.99 (m, 1H), 1.88-1.72 (m, 4H); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 206.6, 140.5, 137.8,

129.9, 129.2, 128.7, 128.6, 127.6, 125.8, 124.0, 120.2, 119.8, 89.9, 86.9, 86.8, 85.0, 79.3, 70.6, 69.4, 54.9, 51.4, 46.4, 34.1, 32.9, 29.8, 29.7, 29.1, 28.7, 28.0, 25.5; EIMS [m/z (%)] 808 (M^+ , 24), 806 (14), 244 (13), 180 (28), 165 (17); HRMS (EI) calcd for $C_{37}H_{36}N_2O_1^{56}Fe^{35}Cl^{191}Ir$: 808.1495; found 808.1512.

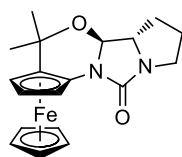
(-)-2-[2*S*_p-(Dimethylhydroxymethyl)ferrocenyl]-1*R*-triethylsilyloxy-7a*S* hexahydro pyrrolo[1,2-*c*]imidazol-3-one (188l**).**



To a solution of *syn*-**187** (1.20 g, 2.72 mmol) in THF (25 mL) at $-78\text{ }^{\circ}\text{C}$ was added *t*-BuLi (5.30 mL, 1.12 M in pentane, 5.98 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with $(\text{CH}_3)_2\text{CO}$ (0.55 mL, 6.80 mmol) and stirred for 30 min. at that temperature. Workup was conducted by addition of water (0.5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether ($2 \times 40\text{ mL}$). The combined organic extract was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.26$) afforded **188l** (537 mg, 1.1 mmol, 36%) as a diastereomerically enriched orange solid; mp $129\text{--}131\text{ }^{\circ}\text{C}$; $[\alpha]_D^{20} -6$ (c 1.0, acetone); IR (KBr) ν_{max} 3302, 3102, 2955, 2910, 2877, 1680, 1469, 1382, 1287 cm^{-1} ; ^1H NMR (300 MHz, acetone- d_6) δ 6.03 (s, 1H), 5.65 (d, 1H, $J = 7.2\text{ Hz}$), 4.48 (t, 1H, $J = 2.1\text{ Hz}$), 4.33 (s, 5H), 4.19 (t, 1H, $J = 2.7\text{ Hz}$), 4.05–3.98 (m, 2H), 3.61–3.54 (m, 1H), 3.11–3.03 (m, 1H), 1.95–1.86 (m, 4H), 1.42 (s, 3H), 1.27 (s, 3H), 0.81 (t, 9H, $J = 8.1\text{ Hz}$), 0.47 (q, 6H, $J = 7.8\text{ Hz}$); ^{13}C NMR (75.5 MHz, acetone- d_6) δ 161.2, 92.9, 91.4, 85.3, 70.4, 68.5, 67.5, 67.3, 63.8, 62.8, 47.3, 32.0, 31.2, 30.6, 26.4, 26.2, 7.0, 5.2; EIMS [m/z (%)] 498 (M^+ , 8), 415 (18), 366 (30), 348 (43), 267 (76), 243 (17); HRMS (EI) calcd

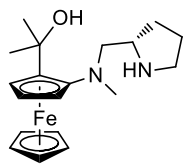
for C₂₅H₃₈N₂O₃Si⁵⁶Fe: 498.2001; found 498.2012. Anal. calcd for C₂₅H₃₈N₂O₃Si⁵⁶Fe: C, 60.23; H, 7.68. Found: C, 60.75, H, 7.77.

**(-)-2-[2S_p-5,5-Dimethyl-ferrocenyl](6a*S*,6b*S*)6b,7,8,9-tetrahydro-5H-pyrrolo
[1',2':3,4]imidazo[5,1-b][1,3]oxazin-11(6aH)-one (215).**



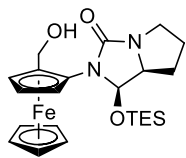
To a solution of **188I** (493 mg, 1.00 mmol) in CHCl₃ (10 mL) at room temperature was added *p*-toluenesulfonic acid monohydrate (380 mg, 2.00 mmol). After stirring for 5 min, a distinct color change from orange to orange-brown was observed. The solution was quenched with saturated aqueous NaHCO₃ (10 mL). The organic layer was washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, *R_f* = 0.20) afforded **215** (158 mg, 0.43 mmol, 32%), as an yellow solid and recovered **188I** (101 mg, 0.20 mmol, 20%); mp 166-167 °C; [α]_D²⁰ = -186 (*c* 1.0, CHCl₃); IR (KBr) ν_{max} 3026, 3009, 2980, 1700, 1507, 1452, 1380, 1400, 1253 cm⁻¹; ¹H NMR (300 MHz, acetone-*d*₆) δ 5.52 (s, 1H), 4.86 (s, 1H), 4.22 (s, 5H), 3.98 (t, 1H, *J* = 4.8 Hz), 3.93 (s, 1H), 3.60-3.44 (m, 2H), 3.03-2.95 (m, 1H), 2.16-2.04 (m, 1H), 1.98-1.85 (m, 2H), 1.82 (s, 3H), 1.68-1.61 (m, 1H), 1.29 (s, 3H); ¹³C NMR (75.5 MHz, acetone-*d*₆) δ 159.2, 93.2, 83.0, 82.1, 75.1, 70.0, 64.3, 63.1, 61.0, 60.3, 46.1, 32.7, 31.1, 29.0, 26.2; EIMS [*m/z* (%)] 366 (*M*⁺, 100), 267 (39), 121 (19), 56 (14); HRMS (EI) calcd for C₁₉H₂₂N₂O₂⁵⁶Fe: 366.1030; found 366.1039. Anal. calcd for C₁₉H₂₂N₂O₂⁵⁶Fe: C, 62.31; H, 6.05. Found: C, 62.38, H, 6.09.

**(-)-2-2S_p-Ferrocenyl-[(*S*)-2-(2-(methyl(pyrrolidin-2-ylmethyl)amino)phenyl)]
propan-2-ol (216).**



To a solution of **215** (20.0 mg, 0.05 mmol) in THF (2 mL) at $-78\text{ }^{\circ}\text{C}$ was added drop-wise a solution of DIBAL-H (0.10 mL, 1.00 M in hexanes, 0.11 mmol). The solution was left to warm up to room temperature for 20 h. The solution was cooled to $0\text{ }^{\circ}\text{C}$ and quenched with sat. aq. potassium sodium tartrate. It was then stirred for 15 min. to separate aqueous and organic layers. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 5:4.6:0.4 EtOAc/hexanes/ Et_3N , $R_f = 0.14$) afforded **216** (15 mg, 0.04 mmol, 76%), as an yellow oil; $[\alpha]_{\text{D}}^{18} = -506$ (c 0.8, CHCl_3); IR (neat) ν_{max} 3548, 3341, 3092, 2967, 2941, 2835, 2778, 1508, 1148 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 4.19 (s, 5H), 3.84 (m, 3H), 3.11 (t, 1H, $J = 5.7$ Hz), 3.01 (m, 1H), 2.91-2.87 (m, 1H), 2.41 (s, 4H), 2.25 (q, 1H, $J = 6.6$ Hz), 1.99-1.93 (m, 1H), 1.86-1.81 (m, 3H), 1.80 (s, 3H), 1.78 (s, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 85.1, 70.0, 69.1, 67.9, 64.9, 63.0, 60.9, 57.5, 54.7, 49.7, 40.8, 30.5, 29.5, 27.1, 22.8; EIMS [m/z (%)] 356 (M^+ , 5), 338 (20), 211 (12), 133 (10), 132 (26), 131 (31); HRMS (EI) calcd for $\text{C}_{19}\text{H}_{28}\text{N}_2\text{O}^{56}\text{Fe}$: 356.1551; found 356.1546.

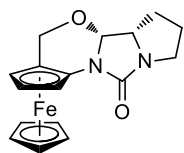
(+)-2-[2S_p-(Hydroxymethyl)ferrocenyl]-1R-triethylsilyloxy-7aS hexahydropyrrolo [1,2-c]imidazol-3-one (217).



To a solution of **188h** (aldehyde above) (780 mg, 0.67 mmol) in MeOH (15 mL) at $0\text{ }^{\circ}\text{C}$ was added NaBH_4 (126 mg, 3.34 mmol) in H_2O (2 mL). After stirring for 30 min, a distinct color change from red-orange to orange was observed. The solution was quenched a solution of NH_4Cl (2 mL). The crude mixture was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7

EtOAc/hexanes, $R_f = 0.20$) afforded **217** (454 mg, 0.96 mmol, 58%) as an orange solid; mp 161-165 °C; $[\alpha]_D^{20} +16$ (c 1.0, acetone); IR (KBr) ν_{\max} 3400, 3084, 2963, 2935, 2906, 1713, 1500, 1394, 1331 cm^{-1} ; ^1H NMR (300 MHz, acetone- d_6) δ 5.63 (d, 1H, $J = 6.0$ Hz), 4.33-4.32 (m, 1H), 4.29 (s, 5H), 4.25-4.24 (m, 1H), 4.19-4.15 (m, 1H), 4.12-4.10 (m, 3H), 4.07 (t, 1H, $J = 2.7$ Hz), 3.50-3.42 (m, 1H), 3.12-3.05 (m, 1H), 2.00-1.96 (m, 2H), 1.86-1.84 (m, 1H), 1.33-1.31 (m, 1H), 0.93 (t, 9H, $J = 8.1$ Hz), 0.68-0.61 (m, 6H); ^{13}C NMR (75.5 MHz, acetone- d_6) δ 159.6, 93.8, 85.7, 85.2, 69.2, 67.6, 64.3, 63.6, 61.6, 57.4, 45.3, 26.6, 25.1, 6.22, 4.7; EIMS [m/z (%)] 470 (M^+ , 3), 338 (82), 149 (25), 121 (33), 103 (100), 97 (12); HRMS (EI) calcd for $\text{C}_{23}\text{H}_{34}\text{N}_2\text{O}_3\text{Si}^{56}\text{Fe}$: 470.1689; found 470.1690.

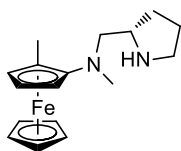
(-)-2-[2*S_p*-Ferrocenyl](6*aR*,6*bS*)-6*b*,7,8,9-tetrahydro-5*H*-pyrrolo[1',2':3,4]imidazo[5,1-*b*][1,3]oxazin-11(6*aH*)-one (218).



To a solution of **217** (450 mg, 0.95 mmol) in CHCl_3 (10 mL) at room temperature was added *p*-toluenesulfonic acid monohydrate (363 mg, 1.91 mmol). After stirring for 5 min, a distinct color change from orange to orange-brown was observed. The solution was quenched with saturated aqueous NaHCO_3 (15 mL). The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.30$) afforded **218** (108 mg, 0.32 mmol, 33%) as an yellow solid; mp 150-152 °C; $[\alpha]_D^{20} = -96$ (c 1.0, acetone); IR (KBr) ν_{\max} 3084, 2976, 2928, 1716, 1503, 1402, 1382, 1257 cm^{-1} ; ^1H NMR (300 MHz, acetone- d_6) δ 5.05 (d, 1H, $J = 7.5$ Hz), 4.82 (d, 1H, $J = 13.2$ Hz), 4.64 (t, 1H, $J = 13.5$ Hz), 4.31 (s, 1H), 4.07-4.01 (m, 7H), 3.92 (d, 1H, $J = 2.4$ Hz), 3.68-3.60 (m, 1H), 3.09-3.01 (m, 1H), 2.11-1.86 (m, 4H); ^{13}C NMR (75.5 MHz, acetone- d_6) δ 160.5, 94.7, 84.0,

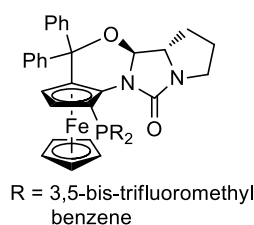
75.7, 70.7, 70.5, 66.9, 63.7, 61.5, 60.9, 56.4, 46.5, 26.4, 25.4; EIMS [m/z (%)] 338 (M^+ , 100), 121 (17), 56 (11); HRMS (EI) calcd for $C_{17}H_{18}N_2O_2^{56}Fe$: 338.0717; found 338.0714. Anal. calcd for $C_{17}H_{18}N_2O_2^{56}Fe$: C, 60.38; H, 5.36. Found: C, 60.29, H, 5.53.

(–)-2-2S_p[(S)-N,2-Dimethyl-N-(pyrrolidin-2-ylmethyl)]ferrocene (219**).**



To a solution of **218** (104 mg, 0.31 mmol) in THF (15 mL) at $-78\text{ }^{\circ}\text{C}$ was added drop-wise a solution of DIBAL-H (1.40 mL, 1.00 M in hexanes, 1.23 mmol). The solution was left to warm up to room temperature for 20 h. As the reaction was incomplete, the reaction mixture was again cooled to $0\text{ }^{\circ}\text{C}$ and another four equivalents of DIBAL-H (1.40 mL) was added to it and stirred for another 5 h at room temperature. The solution was cooled to $0\text{ }^{\circ}\text{C}$ and quenched with sat. aq. potassium sodium tartrate. It was then stirred for 15 min. to separate aqueous and organic layers. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 5:4.6:0.4 EtOAc/hexanes/ Et_3N , $R_f = 0.3$) afforded **219** (80 mg, 0.26 mmol, 82%) as a yellow oil; $[\alpha]_D^{18} = -166$ (c 1.0, $CHCl_3$); IR (neat) ν_{max} 3433, 3386, 3336, 3091, 2963, 2943, 2836, 2782, 1512, 1469, 1210 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 4.03 (s, 5H), 3.87 (s, 1H), 3.73-3.70 (m, 2H), 3.14-3.06 (m, 2H), 3.01-2.95 (m, 1H), 2.68-2.64 (m, 1H), 2.47-2.42 (m, 4H), 2.24 (q, 1H, $J = 9.0$ Hz), 1.99-1.77 (m, 4H), 1.75-1.69 (m, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 109.7, 70.2, 68.4, 65.4, 64.8, 60.1, 57.6, 54.1, 48.4, 40.6, 28.8, 22.9; EIMS [m/z (%)] 312 (M^+ , 100), 200 (47), 121 (87), 77 (49), 56 (58); HRMS (EI) calcd for $C_{17}H_{24}N_2^{56}Fe$: 312.1289; found 312.1289.

(-)-2-[2*S*_p-1-(Bis(3,5-bis(trifluoromethyl)phenyl)phosphino)-5,5-diphenyl-ferrocenyl](6*aS*,6*bS*)-6*b*,7,8,9-tetrahydro-5*H*-pyrrolo[1',2':3,4]imidazo[5,1-*b*][1,3]oxazin-11(6*aH*)-one (**220a**).

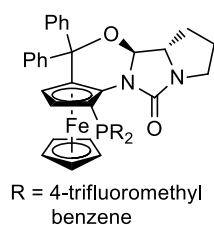


To a solution of *anti*-**194** (300 mg, 0.61 mmol) and TMEDA (0.15 mL, 0.73 mmol) in THF (12 mL) at $-78\text{ }^{\circ}\text{C}$ was added *t*-BuLi (0.60 mL, 1.25 M in pentane, 0.73 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with 1-chloro-3,5-bis-trifluoromethyl benzene (0.30 mL, 0.92 mmol) and stirred for 1 h at that temperature. Workup was conducted by addition of water (0.5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether ($2 \times 20\text{ mL}$). The combined organic extract was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.40$) afforded **220a** (300 mg, 0.32 mmol, 52%) as orange solid; mp $129\text{--}130\text{ }^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{20} = -41$ (*c* 1.0, CHCl_3); IR (KBr) ν_{max} 3090, 3028, 2964, 2925, 1719, 1619, 1475, 1279 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.02–7.97 (m, 3H), 7.80 (s, 1H), 7.72–7.66 (m, 4H), 7.55 (t, 3H, $J = 6.9\text{ Hz}$), 7.47 (t, 1H, $J = 7.2\text{ Hz}$), 7.24–7.20 (m, 2H), 6.92–6.89 (m, 2H), 5.60 (s, 1H), 4.26 (d, 1H, $J = 2.4\text{ Hz}$), 3.87 (dd, 1H, $J = 10.5, 6\text{ Hz}$), 3.65–3.56 (m, 2H), 3.49 (s, 5H), 3.14–3.06 (m, 1H), 2.25–1.89 (m, 3H), 1.97 (m, 1H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 158.5, 146.3, 144.7 (t, $J = 9.1\text{ Hz}$), 141.9 (d, $J = 18.1\text{ Hz}$), 135.5 (d, $J = 26.4\text{ Hz}$), 131.4 (d, $J = 30.2\text{ Hz}$), 128.1 (d, $J = 3.8\text{ Hz}$), 127.8 (d, $J = 4.5\text{ Hz}$), 126.1, 125.1, 124.8, 123.5, 122.0, 121.2, 97.6 (d, $J = 27.9\text{ Hz}$), 85.1 (d, $J = 4.5\text{ Hz}$), 83.4, 82.5, 70.9, 67.7, 66.7, 66.4, 63.8, 45.4, 27.7, 25.6; ^{31}P NMR (242.9 MHz, CDCl_3) -19.1 ; ^{19}F NMR (564.7 MHz,

CDCl₃) –62.8 (d, $J = 16.9$ Hz); FABMS [m/z (%)] 946 (M^+ , 100), 105 (39), 82 (16), 77 (18), 70 (29), 56 (23), 55 (19); HRMS (FAB) calcd for C₄₅H₃₁O₂F₁₂PN₂⁵⁶Fe: 946.1281; found 946.1110. Anal. calcd for C₄₅H₃₁O₂F₁₂PN₂⁵⁶Fe·H₂O: C, 56.03; H, 3.45. Found: C, 56.02, H, 3.38.

(–)-2-[2*S*_p-1-(Bis(4-(trifluoromethyl)phenyl)phosphino)-5,5-diphenyl]

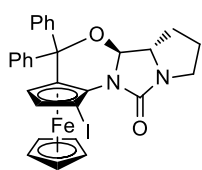
(6*aS*,6*bS*)-6*b*,7,8,9-tetrahydro-5*H*-pyrrolo[1',2':3,4]imidazo[5,1-*b*][1,3]oxazin-11(6*aH*)-one (**220b**).



To a solution of *anti*-**194** (300 mg, 0.61 mmol) and TMEDA (0.15 mL, 0.73 mmol) in THF (10 mL) at –78 °C was added *t*-BuLi (0.70 mL, 1.00 M in pentane, 0.73 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with 1-chloro-4-trifluoromethyl benzene (327 mg, 0.92 mmol) in THF (2 mL) and stirred for 1 h at that temperature. Workup was conducted by addition of water (0.5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether (2 × 20 mL). The combined organic extract was washed with water, brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 2:8 EtOAc/hexanes, $R_f = 0.33$) afforded **220b** (239 mg, 0.29 mmol, 62%) as an glassy orange solid; $[\alpha]_D^{20} = -58$ (c 0.8, CHCl₃); IR (KBr) ν_{\max} 3091, 3060, 3031, 2952, 2923, 2852, 1720, 1466, 1322, 1124 cm^{–1}; ¹H NMR (300 MHz, CDCl₃) δ 7.77–7.63 (m, 6H), 7.56–7.50 (s, 4H), 7.45–7.34 (m, 3H), 7.23–7.20 (m, 3H), 6.99–6.95 (m, 2H), 5.62 (s, 1H), 4.21 (d, 1H, $J = 2.1$ Hz), 3.89–3.79 (m, 2H), 3.71–3.62 (m, 1H), 3.47 (s, 5H), 3.12–3.04 (m, 1H), 2.22–2.11 (m, 2H), 1.96–1.91 (m, 1H), 1.66–1.55 (m, 2H); ¹³C NMR (75.5 MHz, CDCl₃): δ 158.6, 146.6, 145.1,

136.5 (d, $J = 23.4$ Hz), 132.0 (d, $J = 16.6$ Hz), 128.1, 128.0, 127.9, 127.7, 127.6, 126.1, 124.9, 124.5, 96.7, 84.2, 83.5, 82.4, 71.0, 67.5 (d, $J = 5.3$ Hz), 67.1, 63.7, 45.6, 27.7, 25.6; ^{31}P NMR (121.5 MHz, CDCl_3) -20.9 ; ^{19}F NMR (282.4 MHz, CDCl_3) -62.6 (d, $J = 70.6$ Hz); FABMS [$m/z(\%)$] 810 (M^+ , 26), 71 (52), 67 (59), 57 (87), 55 (100), 43 (99), 41 (96); HRMS (FAB) calcd for $\text{C}_{43}\text{H}_{33}\text{O}_2\text{F}_6\text{PN}_2^{56}\text{Fe}$: 810.1533; found 810.1372. Anal. calcd for $\text{C}_{43}\text{H}_{33}\text{O}_2\text{F}_6\text{PN}_2^{56}\text{Fe}$: C, 63.72; H, 4.10. Found: C, 63.03, H, 4.53.

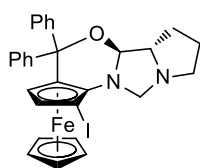
(+)-2-[2*S*_p-1-Iodo-5,5-diphenyl-ferrocenyl](6*aS*,6*bS*)-6*b*,7,8,9-tetrahydro-5H-pyrrolo[1',2':3,4]imidazo[5,1-*b*][1,3]oxazin-11(6*aH*)-one (221).



To a solution of *anti*-**194** (903 mg, 1.84 mmol) and TMEDA (0.45 mL, 2.21 mmol) in THF (20 mL) at -78 °C was added *t*-BuLi (2.00 mL, 1.00 M in pentane, 2.21 mmol). After stirring for 30 min, the reaction mixture became orange-red. The solution was quenched with 1, 2- diiodoethane (779 mg, 2.76 mmol) in THF (2 mL) and stirred for 1 h at that temperature. Workup was conducted by addition of water (0.5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether (2×40 mL). The combined organic extract was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.17$) afforded **221** (824 mg, 1.33 mmol, 73%) as orange solid; mp > 230 °C; $[\alpha]_D^{20} = +4$ (c 3.0, CHCl_3); IR (neat) ν_{max} 3084, 3057, 2963, 2925, 2892, 1718, 1469, 1445, 1377, 1319, 1215, 1175, 1107, 751, 695 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.63-7.61 (d, 2H, $J = 7.5$ Hz), 7.53-7.48 (t, 2H, $J = 7.2$ Hz), 7.44-7.39 (t, 1H, $J = 7.2$ Hz), 7.14-7.13 (m, 3H), 6.91-6.90 (m, 2H), 5.64 (s, 1H), 4.41 (s, 1H), 4.16 (s, 1H), 3.85-3.75 (m, 1H), 3.68 (m, 6H), 3.17-3.11 (t, 1H, $J = 8.4$ Hz), 2.16-2.04 (m, 2H), 1.97-1.95 (m, 1H), 1.69-1.60

(q, 1H, $J = 9.3$ Hz); ^{13}C NMR (75.5 MHz, CDCl_3): δ 159.3, 146.2, 145.3, 127.9, 127.7, 127.5, 126.1, 96.1, 83.6, 82.2, 81.7, 73.5, 72.1, 65.8, 63.5, 45.8, 32.5, 27.0, 25.6; EIMS [m/z (%)] 616 (M^+ , 100), 390 (37), 334 (38), 128 (34), 127 (37), 105 (52), 65 (48); HRMS (EI) calcd for $\text{C}_{29}\text{H}_{25}\text{O}_2\text{N}_2^{56}\text{FeI}$: 616.0310; found 616.0339. Anal. calcd for $\text{C}_{29}\text{H}_{25}\text{O}_2\text{N}_2^{56}\text{FeI}$: C, 56.52; H, 4.09. Found: C, 56.70, H, 4.24.

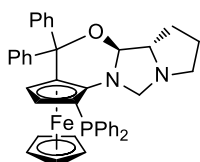
(+)-2-[2*S*_p-1-Iodo-5,5-diphenyl-ferrocenyl](6*aS*,6*bS*)-6*a*,6*b*,7,8,9,11-hexahydro-5H-pyrrolo[1',2':3,4]imidazo[5,1-*b*][1,3]oxazine (222**).**



To a solution of **221** (500 mg, 0.82 mmol) in THF (30 mL) at -78 °C was added drop-wise a solution of DIBAL-H (4.00 mL, 0.90 M in hexanes, 3.25 mmol). The solution was left to warm up to room temperature for 20 h. The reaction mixture was cooled to 0 °C and quenched with sat. aq. potassium sodium tartrate. It was then stirred for 15 min. to separate aqueous and organic layers. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 5:4.5:0.5 EtOAc/hexanes/ Et_3N , $R_f = 0.16$) afforded **222** (277 mg, 0.46 mmol, 57%) as orange solid; mp 198 - 199 °C; $[\alpha]_D^{20} = +141$ (c 3.5, CHCl_3); IR (KBr) ν_{max} 3086, 2965, 2917, 2869, 2842, 1459, 1447, 1105, 1001, 754 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.65 (d, 2H, $J = 8.1$ Hz), 7.48 (t, 2H, $J = 7.2$ Hz), 7.38 (t, 1H, $J = 7.2$ Hz), 7.14-7.09 (m, 3H), 6.97-6.94 (m, 2H), 5.01 (s, 1H), 4.45 (d, 1H, $J = 7.2$ Hz), 4.31 (d, 1H, $J = 2.4$ Hz), 4.00 (d, 1H, $J = 2.4$ Hz), 3.84 (t, 2H, $J = 7.8$ Hz), 3.69 (s, 5H), 3.34-3.29 (m, 1H), 3.02-2.94 (m, 1H), 2.34-2.28 (m, 1H), 1.96-1.81 (m, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 147.1, 145.7, 127.8, 127.6, 127.3, 127.1, 126.3, 101.5, 92.1, 81.7, 81.2, 73.4, 73.0, 69.8, 69.2, 64.7, 56.0, 37.6, 30.7, 26.7; EIMS [m/z (%)] 602 (M^+ , 29), 270 (16), 86 (11), 83

(100), 55 (11); HRMS (EI) calcd for $C_{29}H_{27}IN_2O^{256}Fe$: 602.0517; found 602.0531. Anal. calcd for $C_{29}H_{27}IN_2O^{256}Fe$: C, 57.83; H, 4.52. Found: C, 58.02, H, 4.63.

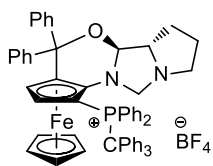
(+)-2-[2*S*_p-1-(Diphenylphosphino)-5,5-diphenyl-ferrocenyl](6*aS*,6*bS*)-6*a*,6*b*,7,8,9,11-hexahydro-5*H*-pyrrolo[1',2':3,4]imidazo[5,1-*b*][1,3]oxazine (223).



To a solution of **222** (153 mg, 0.25 mmol) in THF (3 mL) at $-78\text{ }^{\circ}\text{C}$ was added *n*-BuLi (0.25 mL, 1.50 M in hexanes, 0.37 mmol). After stirring for 1 h, the solution was quenched with 1-chloro-diphenyl phosphine (0.09 mL, 0.50 mmol) and stirred for 1 h at that temperature. Workup was conducted by addition of water (1 mL) and, after warming to room temperature, the reaction mixture was extracted with CH_2Cl_2 (2×20 mL). The combined organic extract was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:6.5:0.5 EtOAc/hexanes/ Et_3N , $R_f = 0.25$) afforded **223** (104 mg, 0.16 mmol, 63%) as an orange solid; mp $114\text{--}115\text{ }^{\circ}\text{C}$; $[\alpha]_D^{20} +160$ (c 1.2, $CHCl_3$); IR (neat) ν_{max} 3054, 2956, 2920, 2849, 1492, 1447, 1432, 1165, 1130, 696 cm^{-1} ; 1H NMR (300 MHz, CD_2Cl_2) δ 7.69–7.67 (m, 2H), 7.64–7.58 (m, 2H), 7.52 (t, 2H, $J = 7.8$ Hz), 7.42–7.32 (m, 9H), 7.23–7.18 (m, 3H), 7.03–7.00 (m, 2H), 5.02 (d, 1H, $J = 0.6$ Hz), 4.11 (d, 1H, $J = 2.7$ Hz), 3.68 (dd, 1H, $J = 2.7, 1.2$ Hz), 3.65–3.60 (m, 1H), 3.55 (s, 5H), 3.52 (s, 2H), 3.05–3.00 (m, 1H), 2.27–2.19 (m, 1H), 1.93–1.68 (m, 3H); ^{13}C NMR (75.5 MHz, CD_2Cl_2) δ 146.7, 140.9 (d, $J = 10.6$ Hz), 134.6 (d, $J = 9.8$ Hz), 135.5 (d, $J = 21.1$ Hz), 132.9 (d, $J = 18.9$ Hz), 129.6, 128.6 (t, $J = 7.5$ Hz), 128.5, 128.0 (d, $J = 7.5$ Hz), 127.6, 127.4, 126.8, 104.9 (d, $J = 23.4$ Hz), 92.7, 84.9 (d, $J = 4.5$ Hz), 81.8, 75.7 (d, $J = 5.3$ Hz), 71.2, 71.1, 70.1, 67.1, 65.8, 56.5, 31.1, 27.0; ^{31}P NMR (121.5 MHz, $CDCl_3$) -24.5 ; EIMS [m/z (%)] 660 (M^+ , 100), 228

(59), 183 (55), 160 (43), 56 (85); HRMS (EI) calcd for $C_{41}H_{37}N_2OP^{56}Fe$: 660.1993; found 660.1991. Anal. calcd for $C_{41}H_{37}N_2OP^{56}Fe$: C, 74.55; H, 5.65. Found: C, 74.03, H, 6.11.

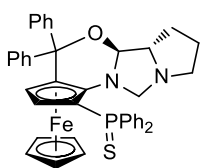
(+)-2-[2*S_p*-5,5-Diphenyl-ferrocenyl](6*aS*,6*bS*)-6*a*,6*b*,7,8,9,11-hexahydro-5*H*-pyrrolo [1',2':3,4]imidazo[5,1-*b*][1,3]oxazin-1-yl)diphenyl(trityl)phosphonium tetrafluoroborate (224**).**



A solution of **223** (66.0 mg, 0.10 mmol) and tritylium tetrafluoroborate (33.0 mg, 0.10 mmol) in CH_2Cl_2 (2 mL) was stirred in a Schlenk flask at room temperature covered from light. The color of the reaction mixture went reddish orange immediately and was stirred for 4 h at room temperature. To the reaction mixture was added Et_2O , the resulting precipitate was filtered, washed with Et_2O (3×5 mL) and dried to get **224** (40 mg, 0.04 mmol, 40 %) as an orange powder. mp 195-196 °C; $[\alpha]_D^{20} +77$ (c 1.5, $CHCl_3$); IR (neat) ν_{max} 3054, 2956, 2920, 2849, 1593, 1492, 1439, 1107, 1047, 644 cm^{-1} ; 1H NMR (300 MHz, CD_2Cl_2) δ 7.93-7.58 (m, 20H), 7.34-7.15 (m, 13H), 6.97 (s, 2H), 5.74 (s, 1H), 4.85 (s, 1H), 4.20 (s, 1H), 3.99 (m, 1H), 3.74 (s, 5H), 3.55 (d, 1H, J = 6.6 Hz), 3.11 (m, 1H), 2.65 (d, 1H, J = 6.0 Hz), 2.33 (m, 1H), 1.99-1.87 (m, 3H), 1.70 (m, 1H); ^{13}C NMR (75.5 MHz, CD_2Cl_2) δ 153.7, 146.1, 145.1, 142.3 (d, J = 5.3 Hz), 136.4, 134.4 (d, J = 11.3 Hz), 131.8 (d, J = 13.6 Hz), 131.0 (d, J = 11.3 Hz), 129.7 (d, J = 2.3 Hz), 129.1, 128.9, 128.7, 128.5, 127.9, 127.5, 126.1, 119.1, 117.8, 101.1, 91.9, 82.3, 77.9, 73.3, 72.9, 72.3, 71.2, 70.5, 70.4 (d, J = 9.1 Hz), 59.1, 57.7, 57.4, 57.1, 30.3, 26.5; ^{31}P NMR (121.5 MHz, $CDCl_3$) 27.5; ^{11}B (96.3 MHz) -1.17; ^{19}F (282.4 MHz) -152.0; MALDI-MS [m/z (%)] 903 (M^+ , 20), 821

(60), 820 (93), 684 (65), 622 (44); HRMS (MALDI-TOF) calcd for $C_{60}H_{52}N_2O^{56}FeP^+$: 903.3166; found 903.3112.

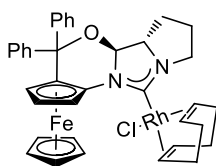
(+)-2-[2*S_p*-5,5-Diphenyl-ferrocenyl](6*aS*,6*bS*)-6*a*,6*b*,7,8,9,11-hexahydro-5H-pyrrolo[1',2':3,4]imidazo[5,1-*b*][1,3]oxazin-1-yl)diphenylphosphine sulphide (225**).**



To a solution of **223** (45.0 mg, 0.07 mmol) in benzene (2 mL) was added sulphur [2.00 mg (recrystallized from benzene), 0.07 mmol] and the solution was heated at reflux for 2 h. Benzene was removed under reduced pressure and the crude mixture was passed through a pad of deactivated silica and washed with EtOAc to obtain **225** (34 mg, 0.05 mmol, 72%) as orange solid. mp 145-146 °C; R_f = 0.15 (3:6.6:0.4 EtOAc/hexanes/Et₃N); $[\alpha]_D^{20}$ = +147 (*c* 3.0, CHCl₃); IR (neat) ν_{max} 3052, 2955, 2916, 2862, 2838, 1479, 1447, 1147, 981 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.98-7.86 (m, 4H), 7.69-7.66 (m, 4H), 7.80 (s, 1H), 7.63 (d, 2H, *J* = 5.4 Hz), 4.34 (dd, 1H, *J* = 7.8, 2.4 Hz), 4.19 (s, 5H), 4.17 (s, 1H), 4.44 (s, 5H), 4.26 (s, 1H), 3.67 (d, 1H, *J* = 8.1 Hz), 3.56 (s, 2H), 2.92-2.89 (m, 1H), 2.79 (t, 1H, *J* = 8.4 Hz), 2.62 (dd, 1H, *J* = 8.7, 2.4 Hz), 1.91-1.84 (m, 2H), 1.49-1.44 (m, 2H), 1.13-1.09 (m, 2H); ¹³C NMR (75.5 MHz, CDCl₃): δ 138.3 (d, *J* = 66.6 Hz), 137.2 (d, *J* = 65.5 Hz), 137.6, 136.8, 133.6, 133.2, 132.9 (d, *J* = 11.0 Hz), 132.1 (d, *J* = 11.2 Hz), 125.1 (s, *J* = 3.6 Hz), 121.7, 109.3 (d, *J* = 8.9 Hz), 77.5, 72.1, 71.9, 71.3, 69.9, 66.4, 65.6 (d, *J* = 10.9 Hz), 65.1, 64.8 (d, *J* = 9.2 Hz), 62.9, 57.8, 55.2, 32.5, 25.8; ³¹P NMR (121.5 MHz, CDCl₃) 43.2; EIMS [*m/z* (%)] 692 (M⁺, 64), 629 (14), 627 (100), 545 (18), 544 (43), 83 (23), 55 (13); HRMS (EI) calcd for C₄₁H₃₇⁵⁶FeN₂OPS: 692.1713; found 692.1705. Anal. calcd for C₄₁H₃₇⁵⁶FeN₂OPS: C, 71.10; H, 5.38. Found: C, 71.15, H, 5.32.

(-)-Chloro[η^4 -1,5-cyclooctadiene]2-[2*S*_p-5,5-diphenyl-ferrocenyl](6*aS*,6*bS*)-

6*a*,6*b*,7,8,9,11-hexahydro-5*H*- pyrrolo[1',2':3,4] imidazol-2-ylidene]rhodium (226).

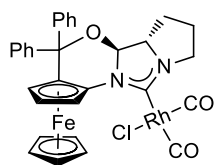


A solution of **195** (80.0 mg, 0.17 mmol) and tritylium tetrafluoroborate (55.0 mg, 0.17 mmol) in CH₂Cl₂ (2 mL) was stirred in a Schlenk flask at room temperature covered from light.

After 5 h, solvent was removed *in vacuo* and the crude solid was washed with dry diethyl ether (3 × 5 mL) and dried *in vacuo*. To this was added Rh(μ-Cl)(cod)]₂ (41.0 mg, 0.08 mmol) and degassed THF (6 mL) in glovebox. The solution was cooled to -78 °C and with increased flow of argon, KO^tBu (19.0 mg, 0.17 mmol) was added at -78 °C and the reaction mixture was allowed to warm to room temperature and stirred for 16 h. The volatiles were removed under reduced pressure and purification of the residue by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, *R_f* = 0.25) afforded **226** (59 mg, 0.08 mmol, 49%) as orange crystalline solid; mp 181-184 °C; [α]_D²⁰ -216 (*c* 1.0, CHCl₃); IR (KBr) ν_{max} 2960, 2916, 2873, 2827, 1523, 1402, 1252 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.67 (d, 2H, *J* = 7.5 Hz), 7.51 (t, 2H, *J* = 7.2 Hz), 7.42 (t, 1H, *J* = 7.2 Hz), 7.14-7.12 (m, 3H), 6.86-6.83 (m, 2H), 6.53 (s, 1H), 5.71 (d, 1H, *J* = 3.6 Hz), 5.23-5.21 (m, 1H), 5.11-5.06 (m, 1H), 4.66-4.57 (m, 1H), 4.27 (s, 1H), 3.96 (m, 2H), 3.81 (s, 5H), 3.67-3.56 (m, 2H), 3.20-3.15 (m, 1H), 2.48-2.17 (m, 5H), 1.99-1.97 (m, 5H), 1.67-1.61 (m, 2H); ¹³C NMR (75.5 MHz, CDCl₃) δ 212.7, 146.5, 144.9, 127.9, 127.8, 127.7, 127.5, 126.2, 100.4, 99.9, 99.8, 88.9, 81.5, 70.9, 70.6, 68.7, 67.3, 67.1, 64.8, 64.3, 62.1, 46.6, 33.1, 32.7, 29.1, 28.6, 28.4, 25.6; FABMS [*m/z* (%)] 810 (M⁺, 2), 95 (50), 91 (36), 67 (70), 55 (100), 43 (99), 39 (54), 29 (73); HRMS (FAB) calcd for C₃₇H₃₈N₂OCiFeRh:

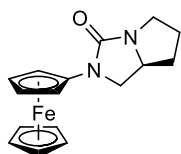
720.1077; found 720.1023. Anal. calcd for $C_{37}H_{38}N_2OCl^{56}FeRh \cdot H_2O$: C, 61.64; H, 5.31. Found: C, 61.06; H, 5.61.

(-)-2-[2*S*_p-(5,5-Diphenyl-ferrocenyl)](6*aS*,6*bS*)-6*a*,6*b*,7,8,9,11-hexahydro-5H-pyrrolo[1',2':3,4]imidazol-2-ylidene)diformylrhodium(IV) chloride (227**).**



A solution of **226** (16.0 mg, 0.02 mmol) in CH_2Cl_2 (1 mL) was bubbled with carbon monoxide for 2 h. The volatiles were removed and purification by flash column chromatography (silicagel, 3:7 EtOAc/hexanes, R_f = 0.44) afforded **227** (12 mg, 0.02 mmol, 92%) as glassy orange solid; $[\alpha]_D^{20}$ -248 (c 0.4, acetone); IR ($CHCl_3$) ν_{max} 3020, 2991, 2929, 2086, 2007, 1527, 1492, 1271 cm^{-1} ; 1H NMR (600 MHz, acetone- d_6) δ 7.85 (d, 2H, J = 7.8 Hz), 7.61 (t, 2H, J = 7.2 Hz), 7.49 (t, 1H, J = 7.2 Hz), 7.21-7.15 (m, 3H), 6.95-6.92 (m, 2H), 6.02 (d, 1H, J = 4.8 Hz), 5.84 (s, 1H), 4.31 (s, 1H), 4.31-4.25 (m, 2H), 4.23 (s, 1H), 3.84 (s, 5H), 3.59-3.54 (m, 1H), 2.46-2.43 (m, 1H), 2.27-2.24 (m, 1H), 2.18-2.15 (m, 1H), 1.85 (m, 1H); ^{13}C NMR (150.9 MHz, acetone- d_6) δ 199.1 (d, J = 40.7 Hz), 186.9 (d, J = 52.8 Hz), 183.0 (d, J = 75.4 Hz), 146.6, 144.8, 128.9, 128.8, 128.8, 128.6, 128.5, 128.4, 127.3, 94.2, 90.0, 84.6, 83.5, 71.2, 70.3, 69.4, 66.3, 65.2, 62.2, 46.4, 27.5, 25.2; FABMS [m/z (%)] 668 (M^+ , 7), 640 (26), 136 (18), 121 (23), 69 (55), 55 (99), 43 (100), 41 (88); HRMS (FAB) calcd for $C_{31}H_{26}N_2O_3Cl^{56}FeRh$: 668.0036; found 667.9966.

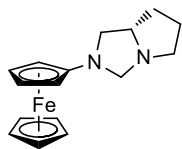
(-)-2-Ferrocenyl-7*aS*-tetrahydropyrrolo[1,2-*c*]imidazol-3-one (229**).**



To a solution of *syn*-**187** (203 mg, 0.46 mmol) in MeOH (4 mL) was added $NaBH_3CN$ (218 mg, 3.57 mmol) and stirred at room temperature. After 1 h, the reaction mixture was cooled to 0 °C and acetic acid (1 mL) was added to it. Removed cold bath, and the reaction mixture was

stirred at room temperature for 16 h. Work up was conducted by washing the organic layer sequentially with sat. aq. NaHCO₃, H₂O, brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 5:5 EtOAc/hexanes, R_f = 0.38) afforded **229** (102 mg, 0.33 mmol, 71%) as an orange solid; mp 98 °C; $[\alpha]_D^{20}$ -10 (c 1.0, CHCl₃); IR (KBr) ν_{\max} 3100, 2965, 2898, 2866, 1699, 1504, 1475, 1417, 1391 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 4.74 (s, 1H), 4.47 (s, 1H), 4.17 (s, 5H), 4.00-3.95 (m, 2H), 3.83-3.69 (m, 3H), 3.50 (d, 1H, J = 7.2 Hz), 3.12-3.09 (m, 1H), 2.04-1.74 (m, 3H), 1.38-1.37 (m, 1H); ¹³C NMR (75.5 MHz, CDCl₃) δ 160.9, 98.6, 68.4, 64.4, 63.8, 58.9, 58.5, 56.3, 48.1, 45.6, 31.1, 25.0; EIMS [m/z (%)] 310 (M^+ , 100), 245 (70), 56 (11), 43 (12); HRMS (EI) calcd for C₁₆H₁₈IN₂O₁⁵⁶Fe: 310.0768; found 310.0764.

(+)-(S)-2-Ferrocenylhexahydro-1H-pyrrolo[1,2-c]imidazole (228).

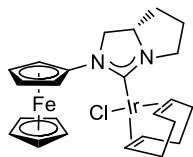


To a solution of *syn*-**187** (500 mg, 1.14 mmol) in THF (60 mL) at -78 °C was added DIBAL-H (7.00 mL, 1.00 M solution in hexanes, 6.82 mmol).

The reaction mixture was allowed to warm to room temperature overnight. After 16 h, the solution was cooled to 0 °C and quenched with sat. aq. potassium sodium tartrate (2 mL) and stirred for another 15 min. to separate organic and aqueous layers. The organic layer was washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 95:5 EtOAc/Et₃N, R_f = 0.20) afforded **228** as an orange crystalline solid (204 mg, 0.69 mmol, 61%); mp 56-57 °C (EtOAc); $[\alpha]_D^{18}$ -12 (c 1.0, CHCl₃); IR (neat) ν_{\max} 3097, 3076, 2959, 2932, 2863, 1507, 1206, 1152, 838 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 4.19 (s, 5H), 3.92 (t, 2H, J = 2 Hz), 3.87 (d, 1H, J = 7.2 Hz),

3.81-3.77 (m, 2H), 3.68 (q, 2H, $J = 2.0$ Hz), 3.22-3.17 (m, 1H), 2.98 (t, 1H, $J = 8.8$ Hz), 2.85 (dd, 1H, $J = 8.8, 4.4$ Hz), 2.75-2.68 (m, 1H), 2.15-2.11 (m, 1H), 1.92-1.77 (m, 2H), 1.69-1.62 (m, 1H); ^{13}C NMR (100.0 MHz, CDCl_3) δ 110.6, 75.2, 67.1, 63.3 (t, $J = 5$ Hz), 56.5, 56.4, 55.8, 55.7, 32.5, 26.1; EIMS [m/z (%)] 296 (100), 227 (20), 213 (38), 186 (19), 121 (27), 84 (12), 83 (71); HRMS (EI) calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2^{56}\text{Fe}$: 296.0976; found 296.0971.

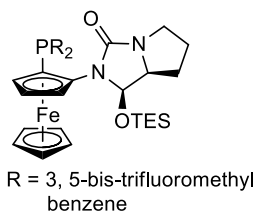
(–)-Chloro [η^4 -1,5-cyclooctadiene] ((*S*)-2-ferrocenylhexahydro-1H-pyrrolo[1,2-*c*]imidazol-2-ylidene)iridium (230**).**



A solution of **228** (45.0 mg, 0.15 mmol) and tritylium tetrafluoroborate (50.0 mg, 0.15 mmol) in CH_2Cl_2 (1.5 mL) was stirred in a Schlenk flask at room temperature covered from light. After 5 h, solvent was removed *in vacuo* and the crude solid was washed with dry diethyl ether (3×5 mL) and dried *in vacuo*. To this was added $\text{Ir}(\mu\text{-Cl})(\text{cod})_2$ (51.0 mg, 0.08 mmol) and degassed THF (3.5 mL) in glovebox. The solution was cooled to -78°C and with increased flow of argon, KOtBu (17.0 mg, 0.15 mmol) was added at -78°C . After 1h, the cold bath was removed and the volatiles were removed under reduced pressure. Purification of the residue by flash column chromatography (silica gel, 3:7 EtOAc/hexanes) afforded a 4:1 mixture of coordination isomers. The minor isomer was found to convert to major in $>95\%$ when stirred in CH_2Cl_2 for 16 h. Data for major isomer **230**: [44 mg, 0.07 mmol, 47%, $R_f = 0.4$ (5:5 EtOAc/hexanes)] as an orange crystalline solid; $[\alpha]_{\text{D}}^{20} -266$ (c 0.5, CHCl_3); IR (KBr) ν_{max} 3448, 3428, 3388, 2956, 2923, 2876, 2830, 1492, 1450, 1261, 1103 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 5.93 (dd, 1H, $J = 2.7, 1.5$ Hz), 4.83-4.77 (m, 1H), 4.67-4.58 (m, 3H), 4.22 (s, 5H), 4.11-4.09 (m, 1H), 4.06-4.04 (m, 1H), 3.94-3.84 (m, 3H), 3.50-3.42

(m, 1H), 3.14-3.12 (m, 1H), 2.79 (td, 1H, $J = 7.2, 4.2$ Hz), 2.16-2.02 (m, 6H), 1.93-1.84 (m, 1H), 1.75-1.42 (m, 6H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 208.6, 100.0, 84.8, 83.9, 69.0, 65.0, 64.9, 64.5, 62.1, 59.4, 55.4, 54.7, 50.9, 47.9, 33.7, 32.9, 31.6, 29.4, 29.2, 24.5; FABMS [m/z (%)] 631 (3), 163 (12), 109 (12), 105 (15), 95 (24); HRMS (EI) calcd for $\text{C}_{24}\text{H}_{31}\text{N}_2^{56}\text{FeIrCl}$: 630.10260; found 630.10430.

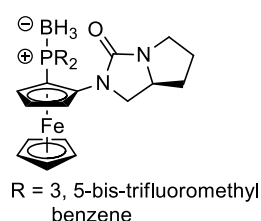
(+)-2-[(2*R*_p-Bis(3,5-bis(trifluoromethyl)phenyl)ferrocenyl]-1*R*-triethylsilyloxy-7*a*S-hexahydropyrrolo[1,2-*c*]imidazol-3-one (231a).



To a solution of *syn*-**187** (200 mg, 0.45 mmol) in THF (5 mL) at –78 °C was added *t*-BuLi (0.80 mL, 1.25 M in pentane, 0.99 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with 1-chloro-3,5-bis-trifluoromethyl benzene (0.36 mL, 1.14 mmol) and stirred for 1 h at that temperature. Workup was conducted by addition of water (0.5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether (2 x 20 mL). The combined organic extract was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 1:9 EtOAc/hexanes, $R_f = 0.30$) afforded **231a** (277 mg, 0.31 mmol, 68%) as a diastereomerically enriched orange solid; mp 53-55 °C; $[\alpha]_{\text{D}}^{20} +271$ (c 1.7, CHCl_3); IR (neat) ν_{max} 3087, 2965, 2881, 2804, 1712, 1616, 1469, 1182 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.08 (d, 2H, $J = 6.3$ Hz), 7.93 (s, 1H), 7.73-7.68 (m, 3H), 5.59 (d, 1H, $J = 6.6$ Hz), 4.58-4.56 (m, 1H), 4.36 (t, 1H, $J = 2.7$ Hz), 3.96 (s, 5H), 3.92-3.88 (m, 2H), 3.59-3.50 (m, 1H), 3.17-3.09 (m, 1H), 1.92-1.81 (m, 2H), 1.72-1.65 (m, 3H), 1.29-1.26 (m, 1H), 0.91 (t, 9H, $J = 10.5$ Hz), 0.66-0.50 (m, 6H); ^{13}C NMR (75.5 MHz,

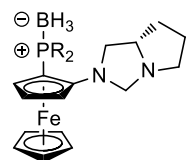
CDCl₃) δ 159.1, 143.0 (t, J = 38.5 Hz), 134.9 (d, J = 23.4 Hz), 131.8 (m, J = 18.1 Hz), 125.0, 123.1, 121.9, 121.4, 100.0 (d, J = 27.9 Hz), 83.2, 70.4, 69.8, 69.6, 68.8 (d, J = 3.8 Hz), 67.6, 66.6 (d, J = 5.3 Hz), 62.5, 46.1, 25.9, 25.3, 6.67, 4.92; ³¹P NMR (121.5 MHz, CDCl₃) –18.9 (d, J = 9.7 Hz); ¹⁹F NMR (282.4 MHz, CDCl₃) –62.8 (d, J = 22.6 Hz); EIMS [m/z (%)] 896 (M⁺, 96), 308 (21), 227 (18), 115 (23), 87 (100), 59 (82); HRMS (EI) calcd for C₃₈H₃₇N₂O₂PSiF₁₂⁵⁶Fe: 896.1519; found 896.1265. Anal. calcd for C₃₈H₃₇N₂O₂PSiF₁₂⁵⁶Fe: C, 50.90; H, 4.16. Found: C, 51.40, H, 4.30.

(+)-2-[2*R_p*-(S)-(Bis(3,5-bis(trifluoromethyl)phenyl)(2-(3-oxotetrahydro-1H-pyrrolo [1,2-*c*]imidazol-2(3H)-yl)phosphonio)ferrocenyl)]trihydroborate (232a).



To a solution of **231a** (660 mg, 0.74 mmol) in THF was added BH₃.THF (1.50 mL, 1.00 M, 1.47 mmol) at 0 °C. Cold bath was removed and the reaction mixture was allowed to warm to room temperature followed by heating to reflux for 4 h. Work up was conducted by addition of water (1 mL) at 0 °C and the reaction mixture was extracted with CH₂Cl₂ (2 x 30 mL). The combined organic extract was washed with water, brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, R_f = 0.36) afforded **232a** (440 mg, 0.58 mmol, 81%) as an orange glassy solid. The compound was found to be unstable to collect data, hence was taken to the next step.

(+)-2-[2*R_p*-(*S*)-(Bis(3,5-bis(trifluoromethyl)phenyl)(2-(tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazol-2(3*H*)-yl)phosphonio)ferrocenyl]trihydroborate (233a**).**

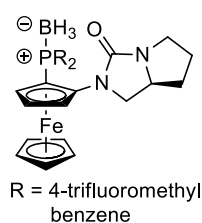


R = 3,5-bis-trifluoromethyl
benzene

To a solution of **232a** (650 mg, 0.88 mmol) in THF (45 mL) at -78°C was added drop-wise a solution of DIBAL-H (6.00 mL, 0.90 M in hexanes, 5.28 mmol). The solution was left to warm up to room temperature for 20 h. The reaction mixture was cooled to 0°C and quenched with sat. aq. potassium sodium tartrate. It was then stirred for 15 min. to separate aqueous and organic layers. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:6.5:0.5 EtOAc/hexanes/ Et_3N , $R_f = 0.60$) afforded **233a** (465 mg, 0.61 mmol, 69%) as an orange solid; mp $203\text{--}205^{\circ}\text{C}$; $[\alpha]_D^{20} = +78$ (c 1.0, CHCl_3); IR (neat) ν_{max} 2972, 2920, 2849, 2362, 2319, 2277, 1460, 1352, 1117 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.00 (s, 1H), 7.90 (d, 2H, $J = 6.9$ Hz), 7.83 (s, 1H), 7.60 (d, 2H, $J = 5.7$ Hz), 4.67 (q, 1H, $J = 4.2$ Hz), 4.29–4.28 (m, 1H), 4.24 (s, 5H), 4.21 (t, 1H, $J = 2.7$ Hz), 3.83–3.74 (m, 2H), 3.35–3.29 (m, 1H), 3.22 (t, 1H, $J = 1.5$ Hz), 3.19–3.13 (m, 1H), 2.90– (1H, $J = 9.0$ Hz), 2.57–2.48 (m, 1H); 2.53–2.51 (m, 1H), 1.95 (m, 2H), 1.69–1.61 (m, 3H), 1.50–1.40 (m, 1H); ^{13}C NMR (75.5 MHz, CDCl_3): δ 140.8, 138.5 (d, $J = 15.8$ Hz), 134.4 (d, $J = 22.6$ Hz), 132.4 (m, $J = 7.5$ Hz), 131.7 (m, $J = 21.8$ Hz), 124.8, 123.9, 122.6, 121.2, 110.4 (d, $J = 20.3$ Hz), 82.4 (d, $J = 19.6$ Hz), 71.0, 68.9, 67.4, 66.6, 64.6, 64.2, 61.2, 56.6, 33.4, 25.3; ^{31}P NMR (121.5 MHz, CDCl_3) -15.2 ; ^{19}F NMR (282.4 MHz, CDCl_3) -63.0 ; ^{11}B NMR (96.29 MHz, CDCl_3) -11.3 ; EIMS [m/z (%)] 766 (M^+ , 3), 669 (11), 103 (62), 86 (11), 84 (100), 75 (48), 57 (41); HRMS (EI) calcd for

$C_{32}H_{28}F_{12}PBN_2^{56}Fe$: 766.1241; found 766.1092. Anal. calcd for $C_{32}H_{28}F_{12}PBN_2^{56}Fe$: C, 50.16; H, 3.68. Found: C, 50.17, H, 3.84.

(+)-2-[2*R_p*-(*S*)-((2-(3-Oxotetrahydro-1*H*-pyrrolo[1,2-*c*]imidazol-2(3*H*)-yl)phenyl)bis(4-(trifluoromethyl)phosphonio)ferrocenyl]trihydroborate (232b**).**

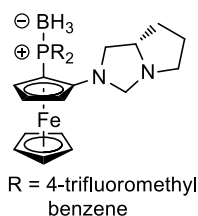


To a solution of *syn*-**187** (1.00 g, 2.27 mmol) in THF (22 mL) at $-78^{\circ}C$ was added *t*-BuLi (5.50 mL, 0.91 M in pentane, 5.00 mmol). After stirring for 30 min, a distinct color change from orange to orange-red was observed. The solution was quenched with 1-chloro-4-trifluoromethyl benzene (2.00 g, 5.67 mmol) in THF (3 mL) and stirred for 1 h at that temperature. Workup was conducted by addition of water (0.5 mL) and, after warming to room temperature, the reaction mixture was extracted with diethyl ether (2×20 mL). The combined organic extract was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 1:9 EtOAc/hexanes, $R_f = 0.30$) afforded an inseparable mixture of starting material and product which was taken to the next step.

To the crude mixture in THF (30 mL) was added $BH_3 \cdot THF$ (9.10 mL, 1.00 M, 9.08 mmol) at $0^{\circ}C$. Cold bath was removed and the reaction mixture was allowed to warm to room temperature followed by heating to reflux for 4 h. Work up was conducted by addition of water (2 mL) at $0^{\circ}C$ and the reaction mixture was extracted with CH_2Cl_2 (2×50 mL). The combined organic extract was washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:7 EtOAc/hexanes, $R_f = 0.47$) afforded **232b** (1.05 g, 1.7 mmol, 70%) as an orange solid; mp $182-184^{\circ}C$; $[\alpha]_D^{20} -38$ (c 1.0, $CHCl_3$); IR (KBr) ν_{max}

3094, 3046, 2963, 2927, 2904, 2420, 2379, 2347, 1689, 1460, 1326, 1130 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.86-7.78 (m, 4H), 7.69 (t, 4H, $J = 14.4$ Hz), 4.55 (s, 2H), 4.38 (s, 5H), 4.28 (s, 1H), 3.50-3.27 (m, 4H), 2.95 (t, 1H, $J = 11.4$ Hz), 1.95-1.90 (m, 2H), 1.77 (m, 2H), 1.38-1.25 (m, 3H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 162.5, 135.0, 134.2, 133.9, 133.8, 133.6, 133.5, 133.3, 132.8, 125.1 (s, $J = 3.8$ Hz), 121.8, 99.2, 71.8 (d, $J = 11.3$ Hz), 71.1, 70.4 (d, $J = 5.3$ Hz), 69.6 (d, $J = 8.3$ Hz), 66.5, 65.6, 55.9, 55.6, 45.3, 32.0, 25.2; ^{31}P (121.5 MHz, CDCl_3) 17.1; ^{11}B NMR (96.3 MHz, CDCl_3) -37.0 ; EIMS [m/z (%)] 630 ($\text{M}^+ - \text{BH}_3$, 51), 86 (84), 84 (100), 49 (27), 47 (28); HRMS (EI) calcd for $\text{C}_{30}\text{H}_{25}\text{N}_2\text{OPF}_6^{56}\text{Fe}$: 630.0958; found 630.0975; Anal. calcd for $\text{C}_{30}\text{H}_{28}\text{OPBN}_2\text{F}_6^{56}\text{Fe} \cdot \text{C}_4\text{H}_8\text{O}$: C, 57.01; H, 5.07. Found: C, 56.77, H, 4.60.

(+)-2-[2*R_p*-(*S*)-(2-(Tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazol-2(3*H*)-yl)-bis(4-(trifluoromethyl)phenyl-phosphonio)ferrocenyl]trihydroborate (233b**).**

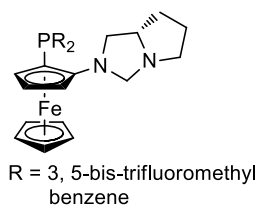


To a solution of **232b** (342 mg, 0.53 mmol) in THF (25 mL) at -78 $^{\circ}\text{C}$ was added drop-wise a solution of DIBAL-H (3.20 mL, 1.00 M in hexanes, 3.18 mmol). The solution was left to warm up to room temperature for 20 h. The reaction mixture was cooled to 0 $^{\circ}\text{C}$ and quenched with sat. aq. potassium sodium tartrate. It was then stirred for 15 min. to separate aqueous and organic layers. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3:6.5:0.5 EtOAc/hexanes/ Et_3N , $R_f = 0.42$) afforded **233b** (215 mg, 0.35 mmol, 64%) as orange solid; mp 182 - 183 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{20} = +69$ (c 0.5, CHCl_3); IR (KBr) ν_{max} 3092, 2979, 2924, 2833, 2367, 2320, 2268, 1469, 1325, 1125 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.66 (d, 2H, $J = 7.8$ Hz), 7.55 (dd, 4H, $J =$

16.5, 7.5 Hz), 7.30 (t, 2H, $J = 6.9$ Hz), 4.77 (dd, 1H, $J = 7.8, 4.8$ Hz), 4.20 (s, 5H), 4.19-4.17 (m, 1H), 4.14 (t, 1H, $J = 2.4$ Hz), 3.81-3.71 (m, 2H), 3.39 (t, 1H, $J = 1.2$ Hz), 3.31-3.26 (m, 1H), 3.10 (t, 1H, $J = 7.2$ Hz), 2.90 (d, 1H, $J = 9.0$ Hz), 2.51 (dt, 1H, $J = 16.5, 6.3$ Hz), 2.25-2.20 (m, 1H), 1.99-1.93 (m, 2H), 1.67-1.64 (m, 2H), 1.53-1.49 (m, 2H); ^{13}C NMR (150.9 MHz, CDCl_3): δ 142.8 (d, $J = 15.1$ Hz), 140.5 (d, $J = 12.1$ Hz), 135.3 (d, $J = 21.1$ Hz), 132.5 (d, $J = 18.8$ Hz), 131.7 (q, $J = 31.7$ Hz), 130.5 (q, $J = 31.7$ Hz), 126.7, 125.1 (d, $J = 18.1$ Hz), 124.8 (d, $J = 13.6$ Hz), 123.0 (d, $J = 12.1$ Hz), 110.1 (d, $J = 21.1$ Hz), 82.2 (d, $J = 21.1$ Hz), 71.0, 68.8, 68.1, 65.8, 64.4, 63.2, 63.0, 56.6, 33.5, 25.4; ^{31}P NMR (121.5 MHz, CDCl_3) -19.3 ; ^{11}B NMR (96.29 MHz, CDCl_3) -12.0 ; EIMS [m/z (%)] 616 ($\text{M}^+ - \text{BH}_3$, 100), 296 (19), 84 (25), 83 (58), 82 (29), 57 (10), 55 (17); HRMS (EI) calcd for $\text{C}_{30}\text{H}_{27}\text{F}_6\text{PN}_2^{56}\text{Fe}$: 616.1165; found 616.1170. Anal. calcd for $\text{C}_{30}\text{H}_{27}\text{F}_6\text{PN}_2^{56}\text{Fe}$: C, 57.18; H, 4.80. Found: C, 57.34, H, 4.90.

(+)-2-[2*R_p*-(*S*)-2-(2-(Bis(3,5-bis(trifluoromethyl)phenyl)phosphine)ferrocenyl]

hexahydro-1*H*-pyrrolo[1,2-*c*]imidazole (234a).

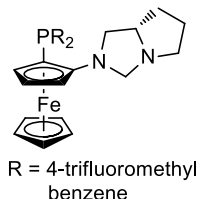


To a solution of **233a** (100 mg, 0.13 mmol) in benzene (2 mL) was added DABCO (15.0 mg, 0.13 mmol) and the solution was heated to reflux for 2 h. Benzene was removed under reduced pressure and the crude mixture was passed through a pad of deactivated silica and washed with EtOAc to obtain **234a** (90 mg, 0.12 mmol, 92%) as an orange solid. mp 53-54 °C; $R_f = 0.33$ (9.6:4 EtOAc/ Et_3N); $[\alpha]_D^{20} = +27$ (c 1.3, CHCl_3); IR (KBr) ν_{max} 3096, 2965, 2923, 2872, 2826, 1466, 1356, 1279, 1134 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3) δ 7.98 (s, 1H), 7.89 (d, 2H, $J = 6.6$ Hz), 7.80 (s, 1H), 7.63 (d, 2H, $J = 5.4$ Hz), 4.34 (dd, 1H, $J = 7.8, 2.4$ Hz), 4.19 (s, 5H), 4.17 (s, 1H), 4.12 (t, 1H, $J = 2.4$ Hz), 3.77 (d, 1H, $J = 7.8$

Hz), 3.74-3.70 (m, 1H), 3.11 (s, 1H), 3.07-3.04 (m, 1H), 3.02 (t, 1H, $J = 7.8$ Hz), 2.89 (dd, 1H, $J = 8.4, 3.0$ Hz), 2.21 (q, 1H, $J = 6.6$ Hz), 2.08-2.04 (m, 1H), 1.69-1.63 (m, 2H), 1.49-1.43 (m, 1H); ^{13}C NMR (150.9 MHz, CDCl_3): δ 141.3 (d, $J = 19.6$ Hz), 139.3 (d, $J = 18.1$ Hz), 134.6 (d, $J = 21.1$ Hz), 131.8 (m, $J = 15.1$ Hz), 125.8, 124.0 (d, $J = 7.5$ Hz), 123.7, 122.2, 122.1 (d, 1H, $J = 7.5$ Hz), 113.0 (d, $J = 19.6$ Hz), 76.2 (d, $J = 19.6$ Hz), 68.4, 67.0, 66.2, 63.5 (d, $J = 3.0$ Hz), 62.4, 56.9, 56.1, 32.7, 26.0; ^{31}P NMR (242.9 MHz, CDCl_3) -13.0 ; ^{19}F NMR (564.7 MHz, CDCl_3) -62.9 (d, $J = 118.6$ Hz); EIMS [$m/z(\%)$] 752 (M^+ , 26), 115 (14), 86 (44), 83 (62), 71 (42), 58 (53), 57 (100); HRMS (EI) calcd for $\text{C}_{32}\text{H}_{25}\text{F}_{12}\text{PN}_2^{56}\text{Fe}$: 752.0913; found 752.0903.

(+)-2-[2*R_p*-(*S*)-2-(2-(bis(4-(Trifluoromethyl)phenyl)phosphino)ferrocenyl]

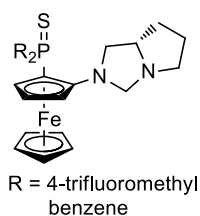
hexahydro-1H-pyrrolo[1,2-*c*]imidazole (234b).



A solution of **233b** (75.0 mg, 0.12 mmol) in Et_2NH (2 mL) was stirred at room temperature for 4 h. The volatiles were removed under reduced pressure and the crude mixture was passed through a pad of deactivated silica and washed with EtOAc to obtain **234b** (55 mg, 0.09 mmol, 75%) as an orange solid. $R_f = 0.25$ (3:7 EtOAc/hexanes); mp 97-98 °C; $[\alpha]_D^{20} = +78$ (c 1.4, CHCl_3); IR (KBr) ν_{max} 3118, 3092, 3041, 2961, 2923, 1462, 1324, 1125 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.66-7.50 (m, 6H), 7.34-7.29 (m, 2H), 4.35 (dd, 1H, $J = 7.5, 2.4$ Hz), 4.16 (s, 5H), 4.06 (d, 2H, $J = 2.1$ Hz), 3.80 (d, 1H, $J = 7.8$ Hz), 3.73-3.65 (m, 1H), 3.27 (s, 1H), 3.06-2.97 (m, 2H), 2.92 (dd, 1H, $J = 9.0, 3.6$ Hz), 2.31-2.22 (m, 1H), 2.09-1.99 (m, 1H), 1.72-1.44 (m, 3H); ^{13}C NMR (75.5 MHz, CDCl_3): δ 141.5 (d, $J = 15.8$ Hz), 141.4 (d, $J = 13.6$ Hz), 135.5 (d, $J = 21.9$ Hz), 132.4 (m, $J = 9.1$ Hz), 131.7, 131.3, 130.4, 130.0, 125.9, 125.0 (s, $J = 3.8$ Hz), 122.3, 113.3 (d, $J = 18.9$ Hz), 76.3, 76.0,

68.3, 67.6, 65.4, 62.3, 61.0 (d, $J = 9.8$ Hz), 57.1 (d, $J = 3.0$ Hz), 55.8, 32.7, 26.0; ^{31}P NMR (242.9 MHz, CDCl_3) -16.5 ; ^{19}F NMR (564.7 MHz, CDCl_3) -62.7 (d, $J = 22.6$ Hz); EIMS [$m/z(\%)$] 616 (M^+ , 80), 296 (21), 86 (59), 84 (100), 57 (29), 55 (33), 43 (25); HRMS (EI) calcd for $\text{C}_{30}\text{H}_{27}\text{F}_6\text{PN}_2^{56}\text{Fe}$: 616.1165; found 616.1172. Anal. calcd for $\text{C}_{30}\text{H}_{27}\text{F}_6\text{PN}_2^{56}\text{Fe}$: C, 58.46; H, 4.42. Found: C, 58.75, H, 4.80.

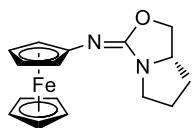
(+)-2-[2*R_p*-(*S*)-(2-(Tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazol-2(3*H*)-yl)bis(4-(trifluoromethyl)phosphono)ferrocenyl)sulphide (235).



To a solution of **234b** (45.0 mg, 0.07 mmol) in benzene (2 mL) was added sulphur [2.00 mg (recrystallized from benzene), 0.07 mmol] and the solution was heated at 50 °C for 18 h. Benzene was removed under reduced pressure and the crude mixture was passed through a pad of deactivated silica and washed with EtOAc to obtain **235** (34 mg, 0.05 mmol, 72%) as glassy orange solid. $R_f = 0.10$ (3:7 EtOAc/hexanes); $[\alpha]_D^{20} = -50$ (c 1.0, CHCl_3); IR (KBr) ν_{max} 3097, 2972, 2928, 2851, 1458, 1398, 1318, 1160, 1056 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.98-7.86 (m, 4H), 7.69-7.66 (m, 4H), 7.80 (s, 1H), 7.63 (d, 2H, $J = 5.4$ Hz), 4.34 (dd, 1H, $J = 7.8, 2.4$ Hz), 4.19 (s, 5H), 4.17 (s, 1H), 4.44 (s, 5H), 4.26 (s, 1H), 3.67 (d, 1H, $J = 8.1$ Hz), 3.56 (s, 2H), 2.92-2.89 (m, 1H), 2.79 (t, 1H, $J = 8.4$ Hz), 2.62 (dd, 1H, $J = 8.7, 2.4$ Hz), 1.91-1.84 (m, 2H), 1.49-1.44 (m, 2H), 1.13-1.09 (m, 2H); ^{13}C NMR (75.5 MHz, CDCl_3): δ 138.3 (d, $J = 66.6$ Hz), 137.2 (d, $J = 65.5$ Hz), 137.6, 136.8, 133.6, 133.2, 132.9 (d, $J = 11.0$ Hz), 132.1 (d, $J = 11.2$ Hz), 125.1 (s, $J = 3.6$ Hz), 121.7, 109.3 (d, $J = 8.9$ Hz), 77.5, 72.1, 71.9, 71.3, 69.9, 66.4, 65.6 (d, $J = 10.9$ Hz), 65.1, 64.8 (d, $J = 9.2$ Hz), 62.9, 57.8, 55.2, 32.5, 25.8; ^{31}P NMR (121.5 MHz, CDCl_3) 43.2; ^{19}F NMR (282.4 MHz, CDCl_3) -63.1 (d, $J = 6.8$ Hz); EIMS [m/z (%)] 648 (M^+ , 53), 615

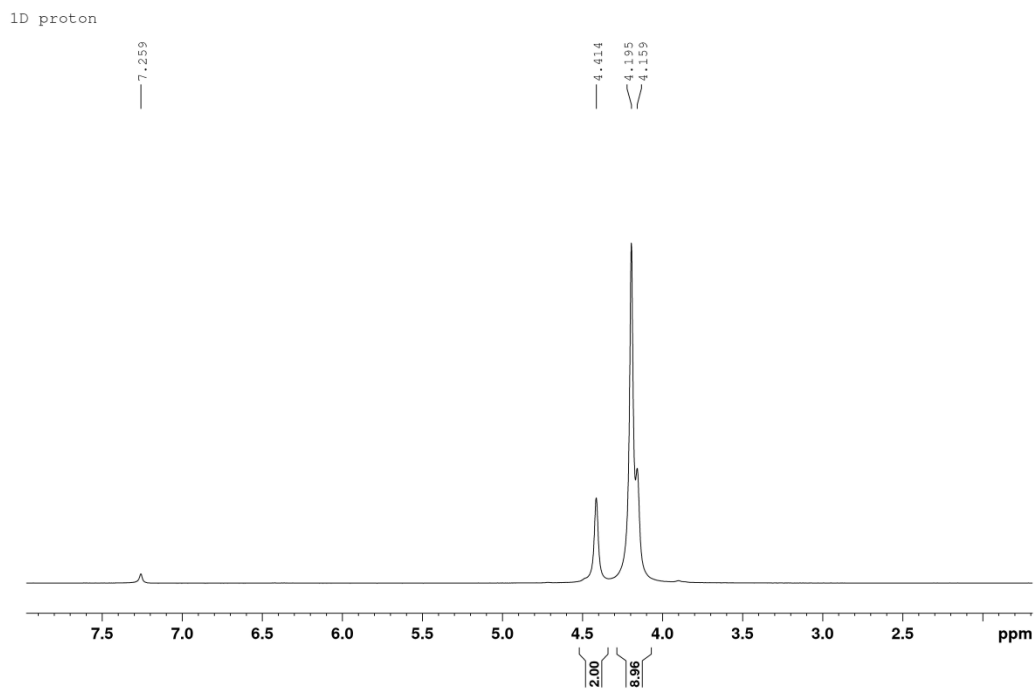
(42), 295 (11), 149 (25), 83 (100), 57 (86), 43 (88); HRMS (EI) calcd for $C_{30}H_{27}SF_6PN_2^{56}Fe$: 648.0886; found 648.0873.

(-)-(S,E)-N-Ferrocenyl-(tetrahydropyrrolo[1,2-c]oxazol-3(1H)-ylidene)amine (237).

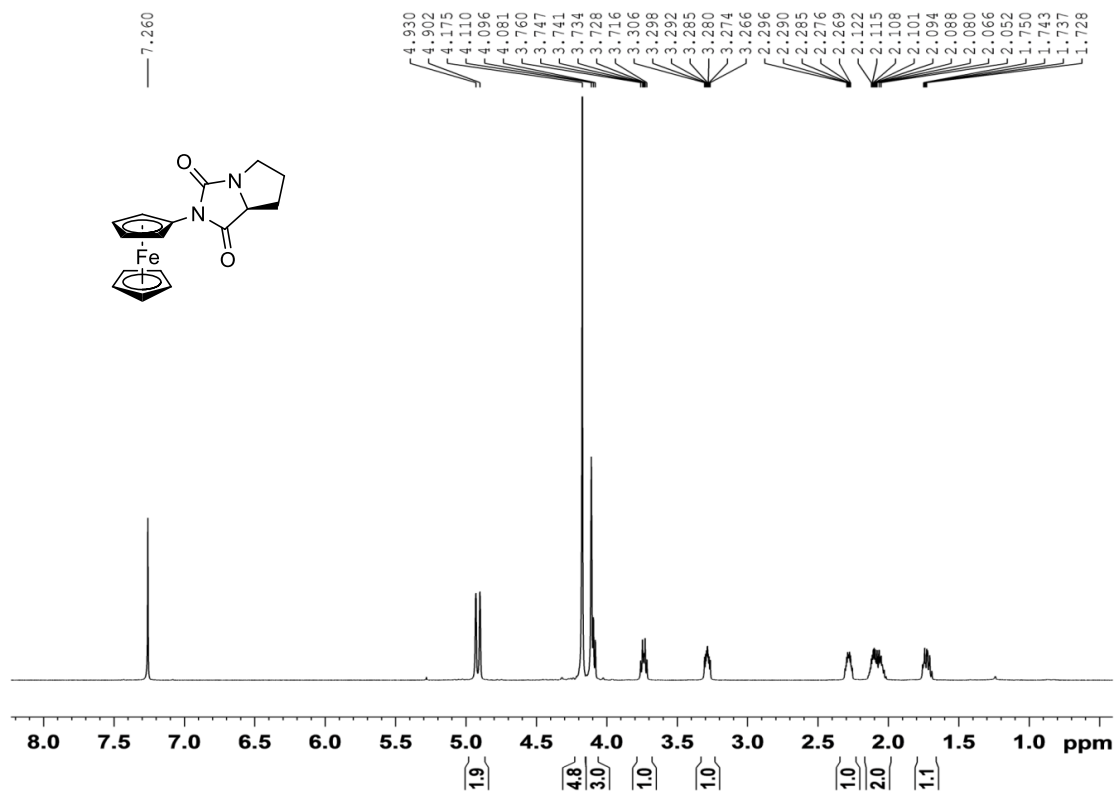


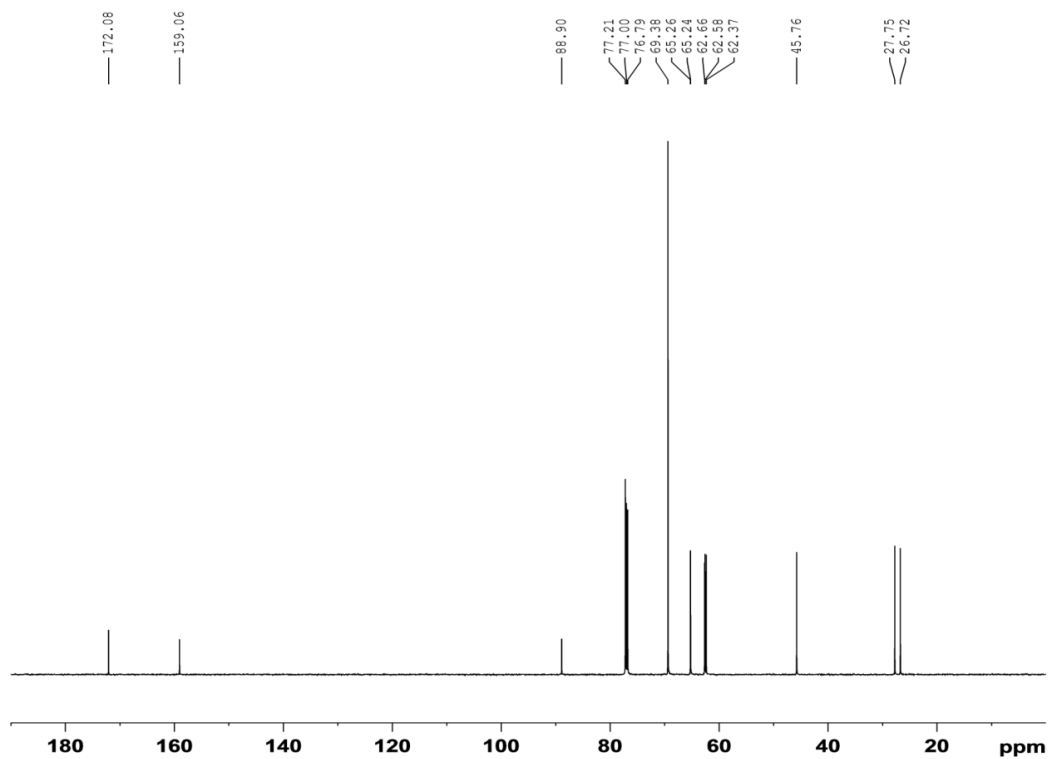
A solution of **190a** (50.0 mg, 0.15 mmol) in $POCl_3$ (1.5 mL) was stirred at room temperature. After 16 h, $POCl_3$ was removed under reduced pressure and the crude mixture was passed through a pad of deactivated silica and washed with EtOAc to obtain **237** (26 mg, 0.08 mmol, 56%) as an orange solid. mp 107-109 °C; R_f = 0.43 (9.6:0.4 EtOAc/Et₃N); $[\alpha]_D^{20}$ = -44 (*c* 0.9, $CHCl_3$); IR (neat) ν_{max} 3089, 2970, 2925, 2902, 2858, 1655, 1478, 1180, 812 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 4.59 (t, 1H, J = 8.4 Hz), 4.41 (s, 1H), 4.31 (s, 1H), 4.19 (dd, 1H, J = 8.4, 4.0 Hz), 4.09 (s, 5H), 3.94 (t, 2H, J = 2.0 Hz), 3.92-3.87 (m, 1H), 3.71-3.64 (m, 1H), 3.29-3.23 (m, 1H), 2.05-1.99 (m, 3H), 1.48-1.42 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 157.6, 101.9, 70.5, 68.9, 64.7, 64.6, 64.5, 63.8, 60.2, 49.0, 30.7, 26.1; EIMS [m/z (%)] 310 (M^+ , 63), 227 (38), 149 (20), 85 (64), 83 (100), 55 (22); HRMS (EI) calcd for $C_{16}H_{18}^{56}FeN_2O$: 310.0768; found 310.0767.

6. Selected Spectra

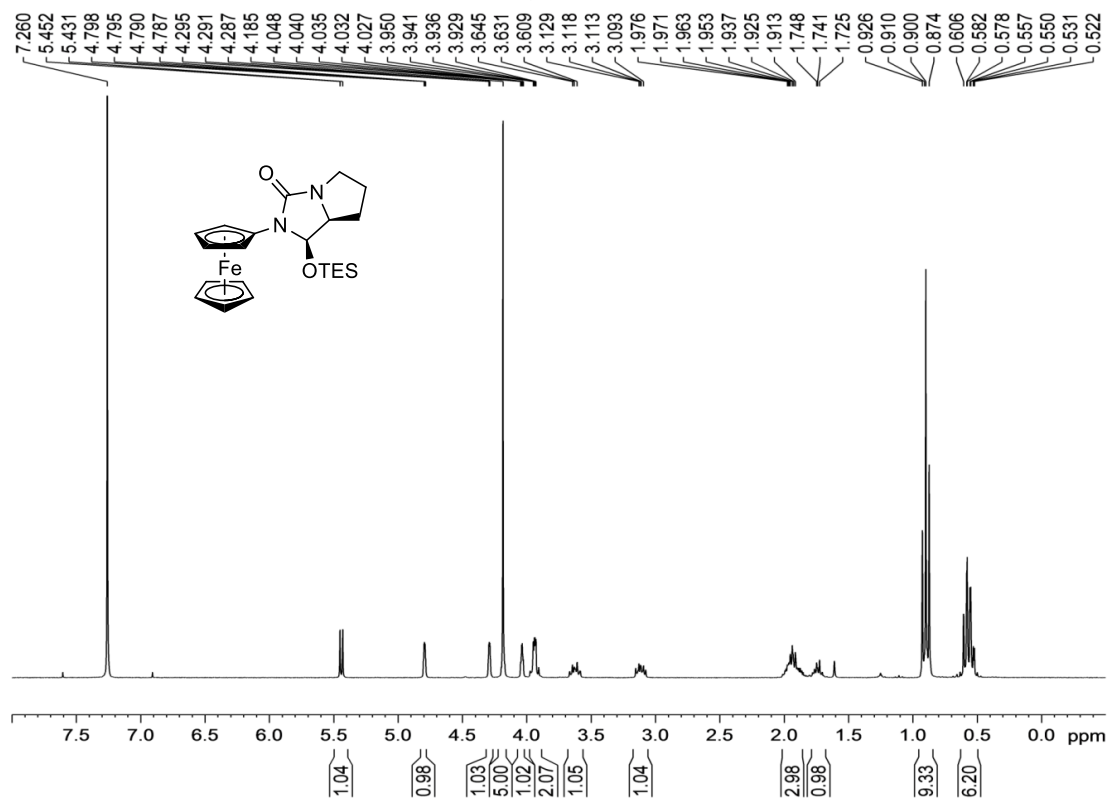


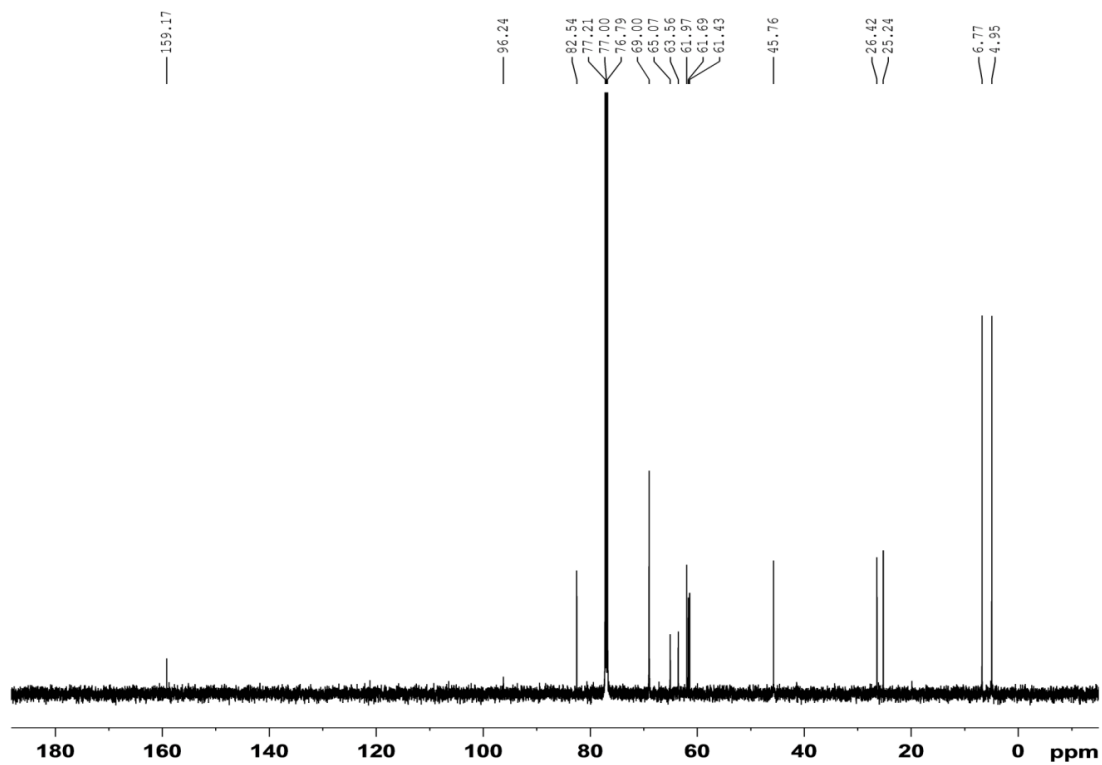
^1H NMR showing 5:1 mixture of FcI:Fc.



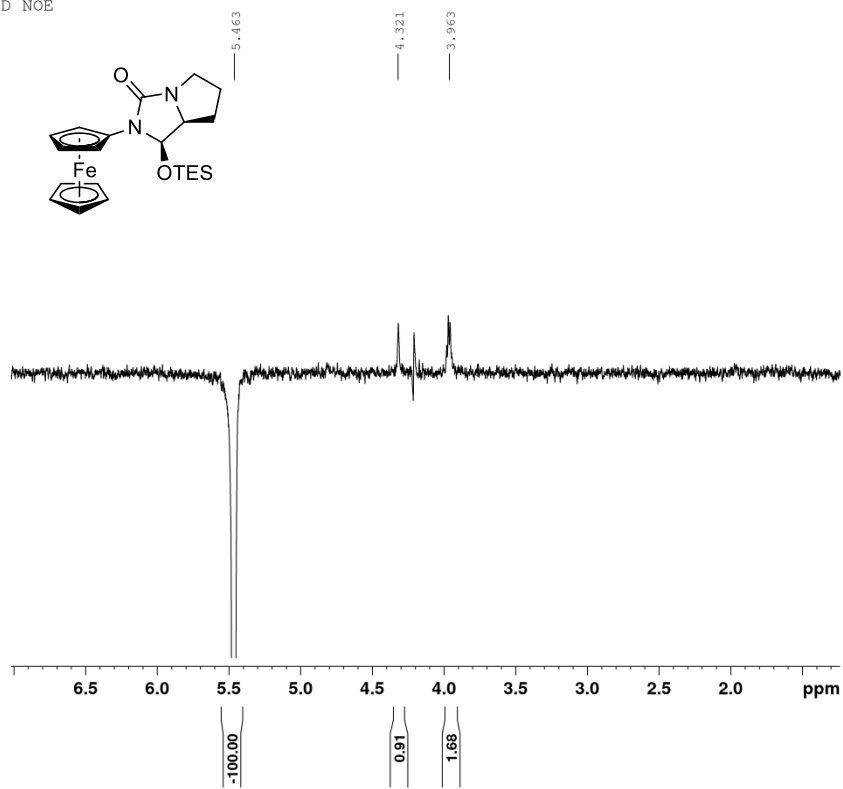


^1H and ^{13}C spectra for **185**.

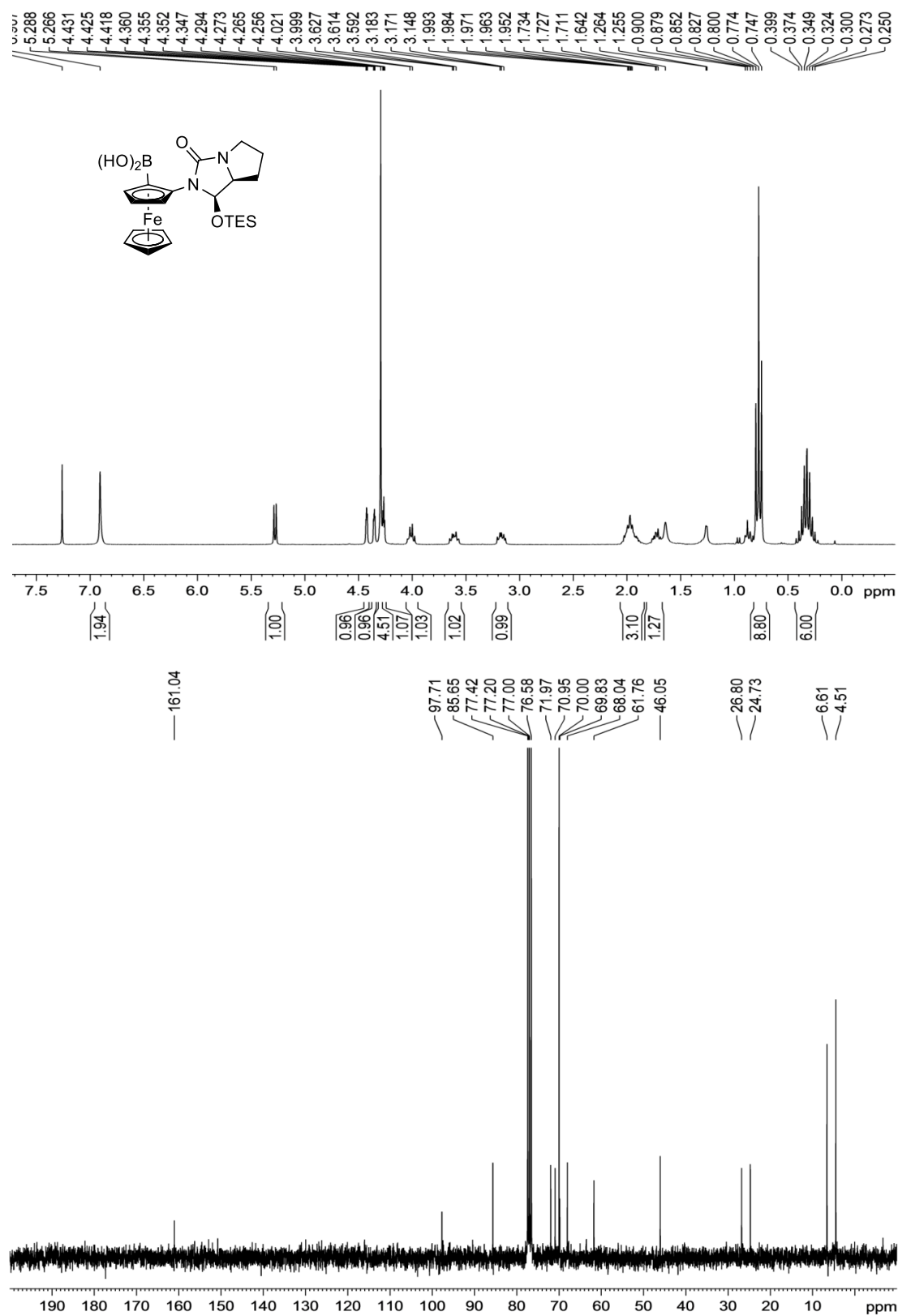


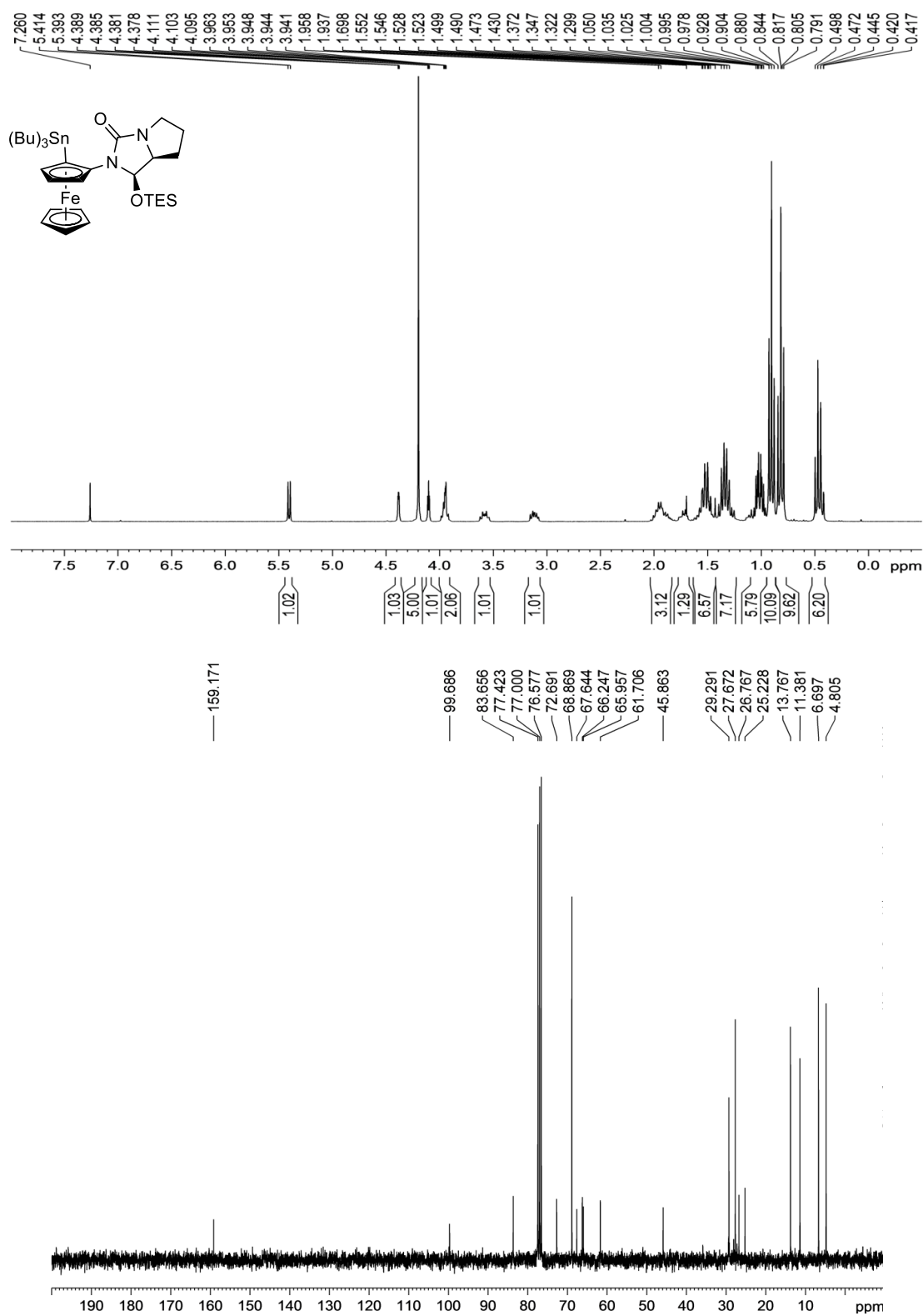


1D NOE

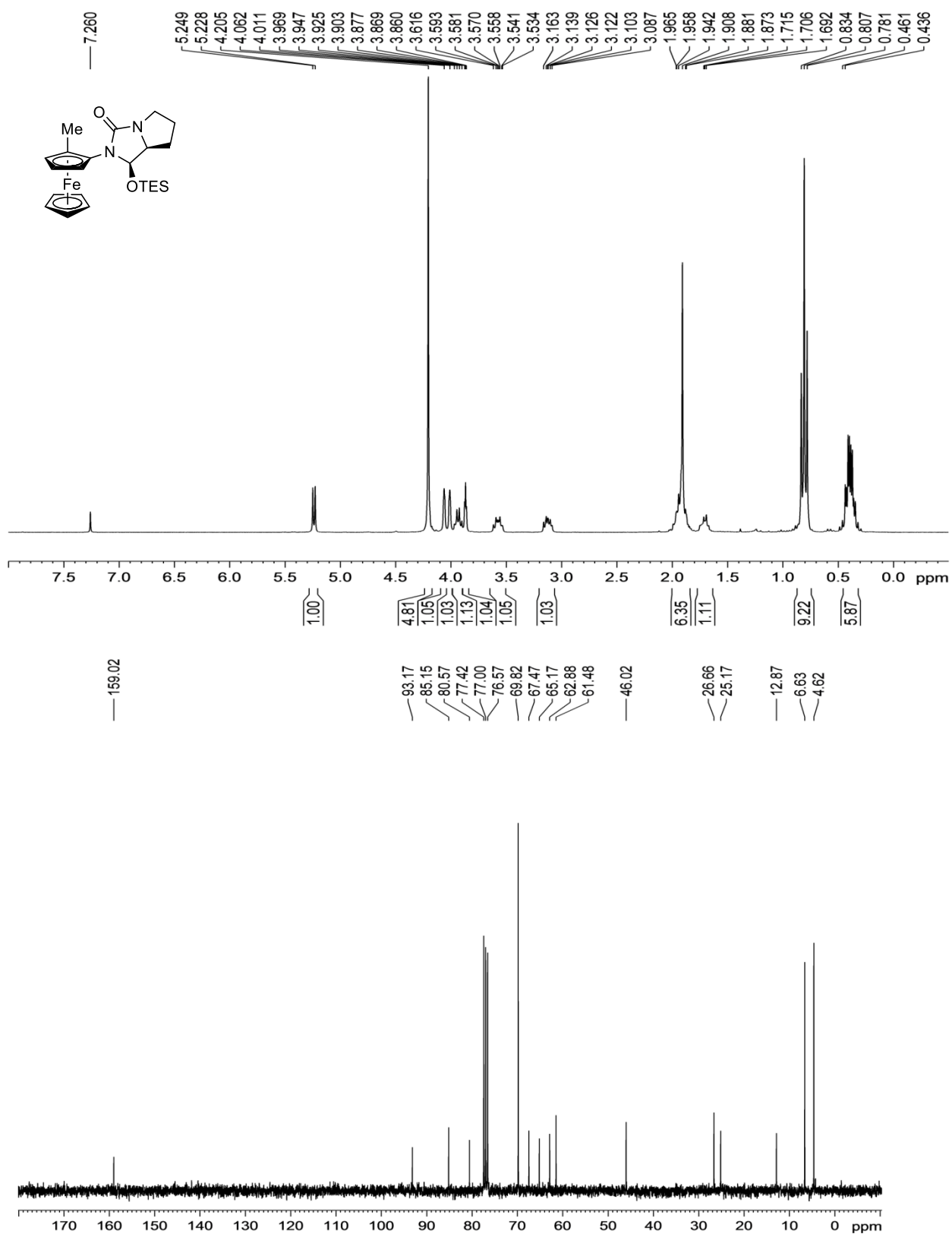


^1H , ^{13}C and nOe spectra for *syn*-187.

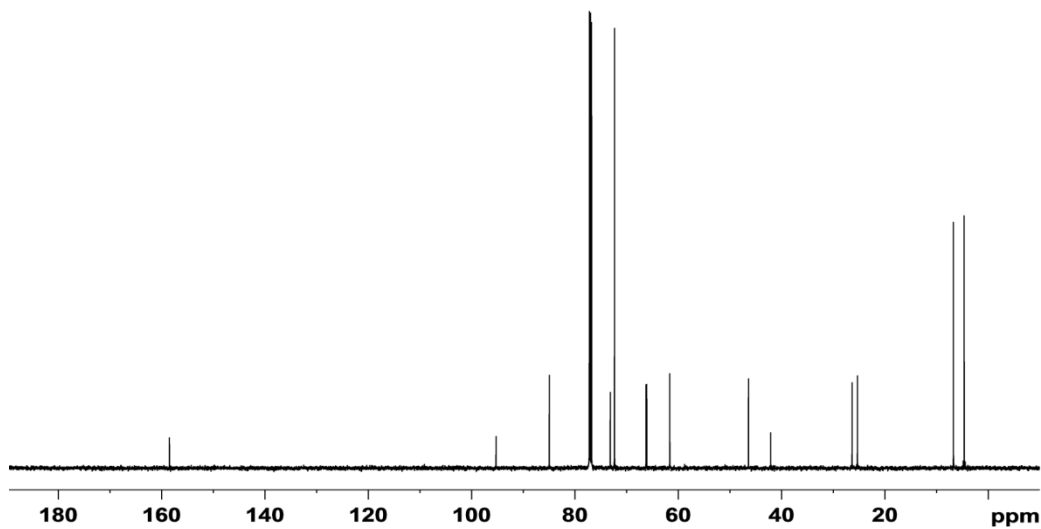




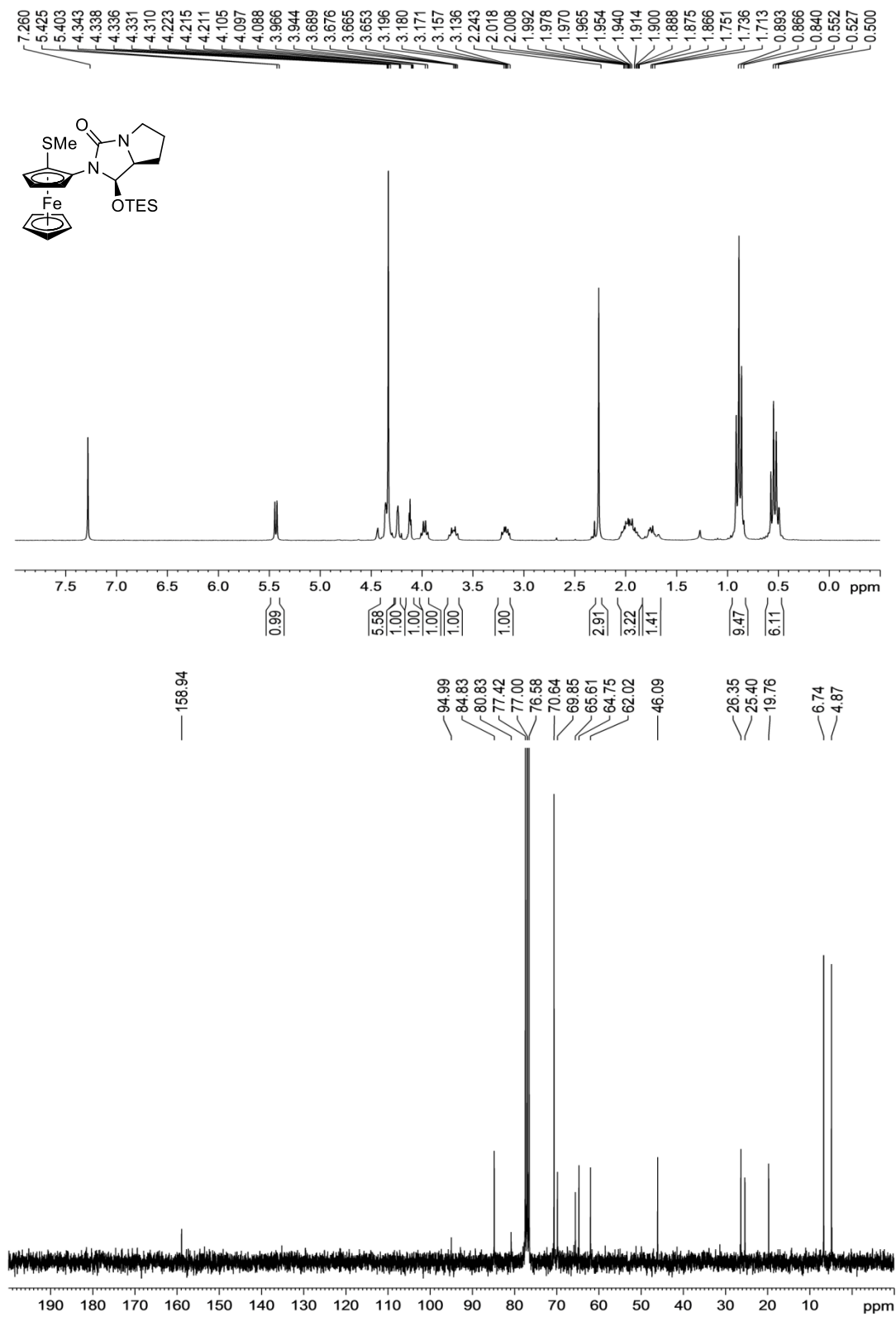
^1H and ^{13}C spectra for **188c**.



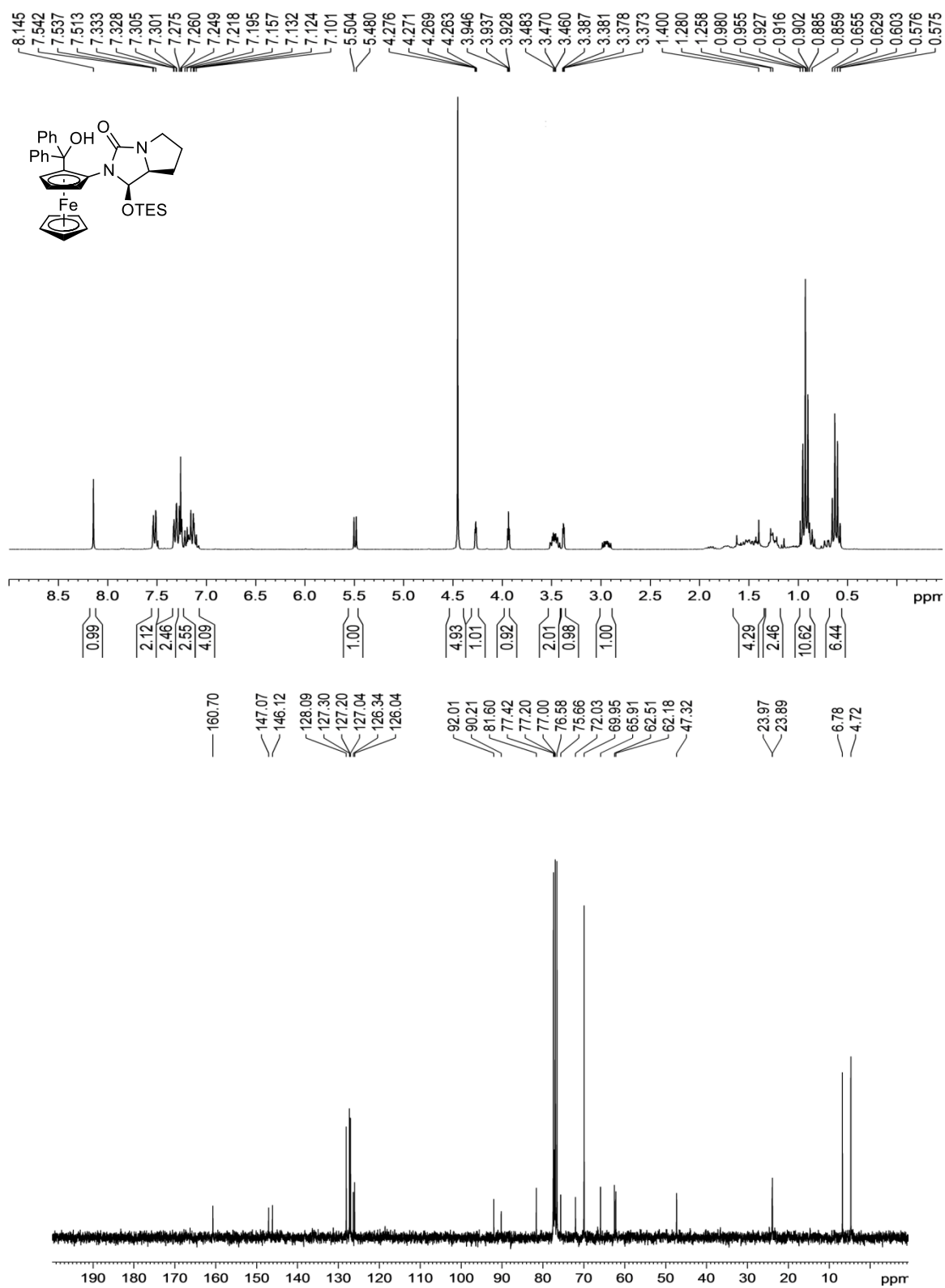
^1H and ^{13}C spectra for **188d**.



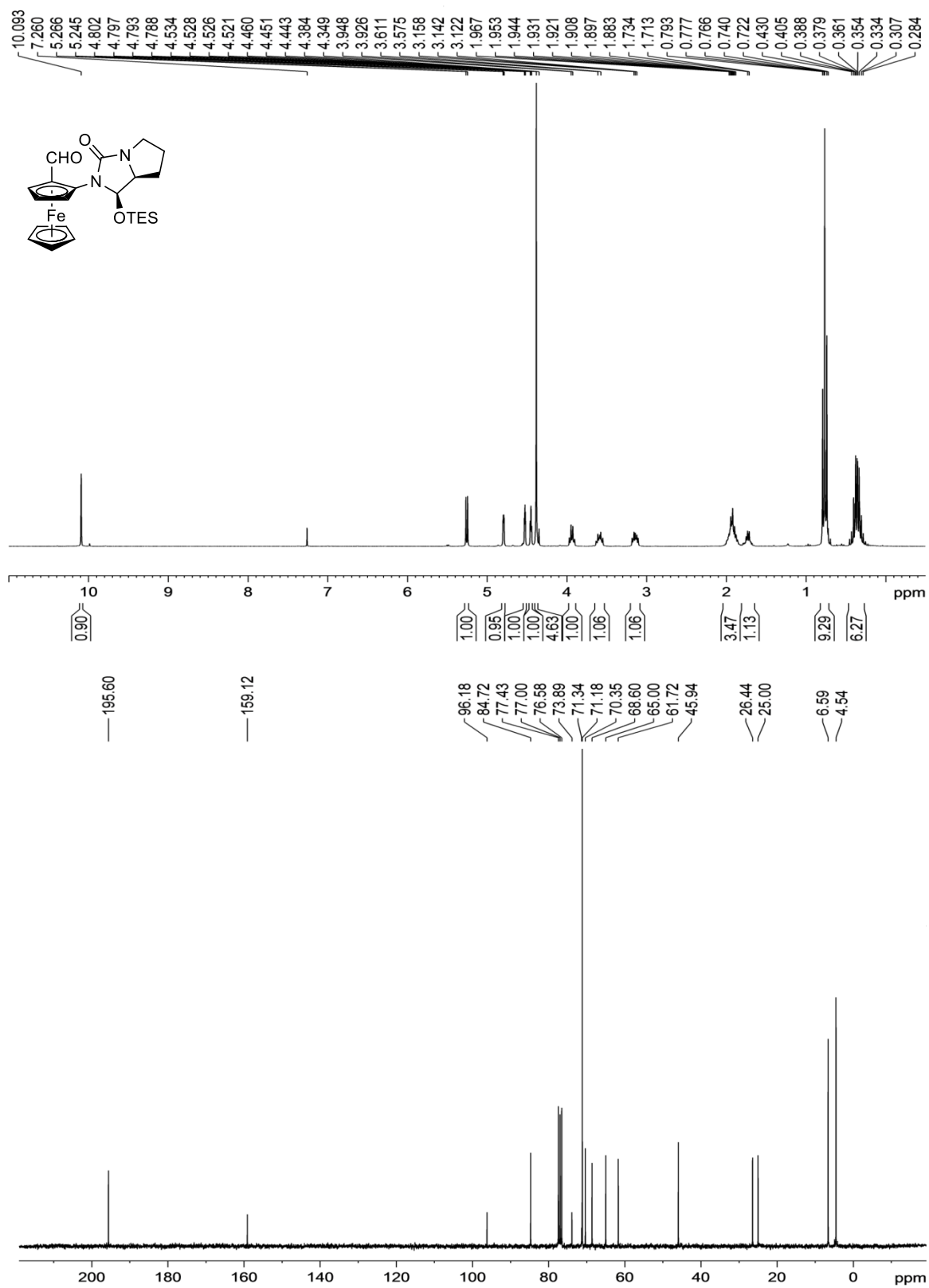
192



^1H and ^{13}C spectra for **188f**.

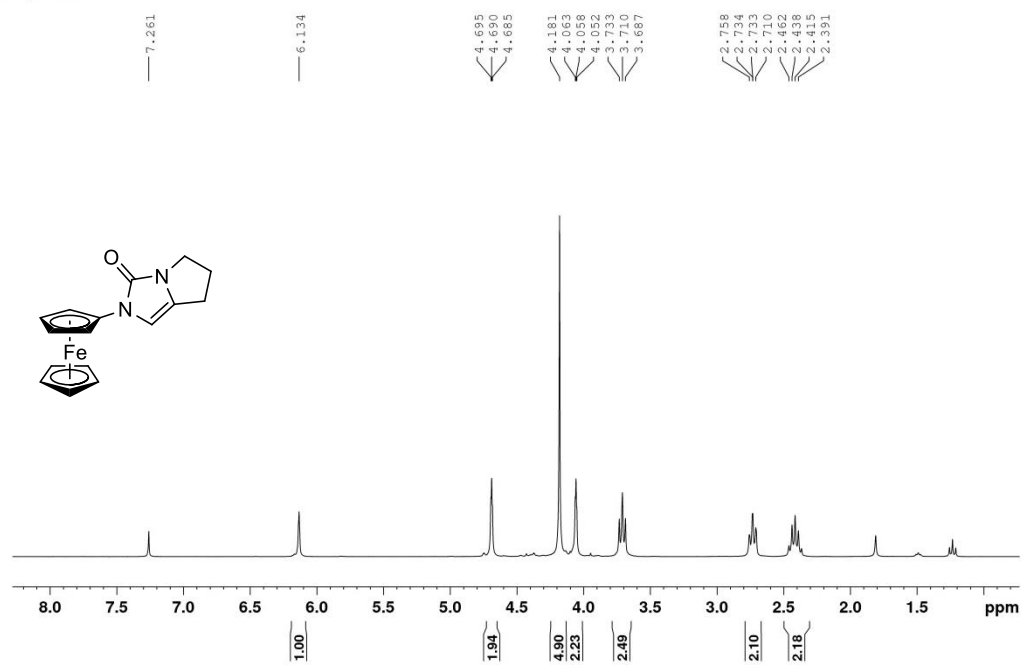


¹H and ¹³C spectra for 188g.

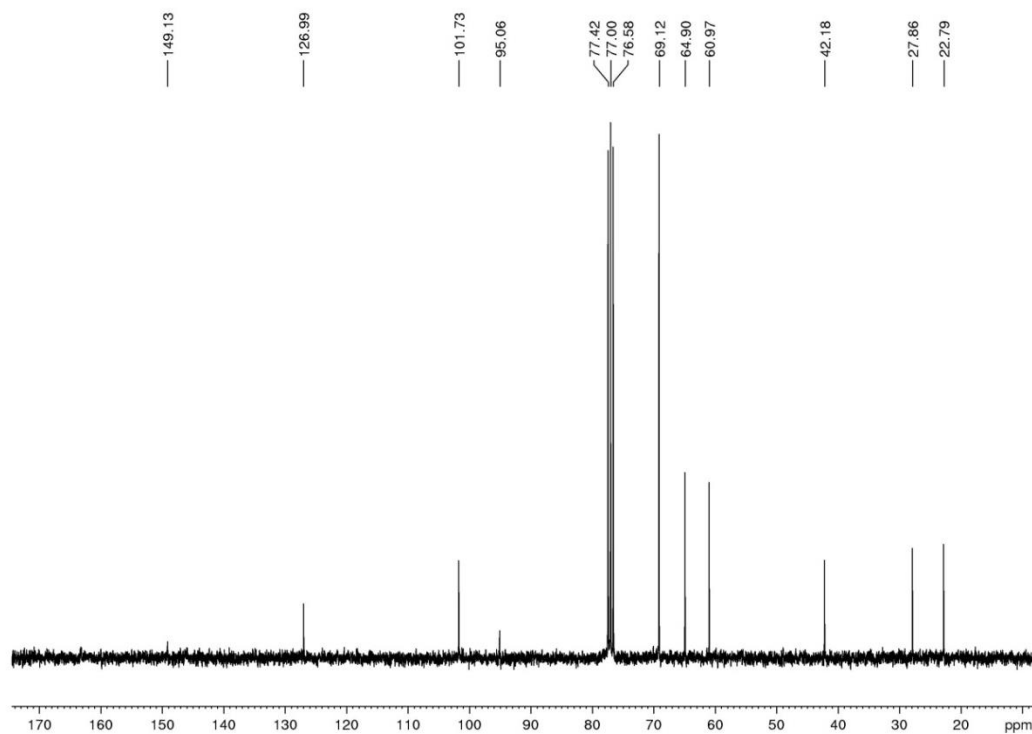


¹H and ¹³C spectra for **188h**.

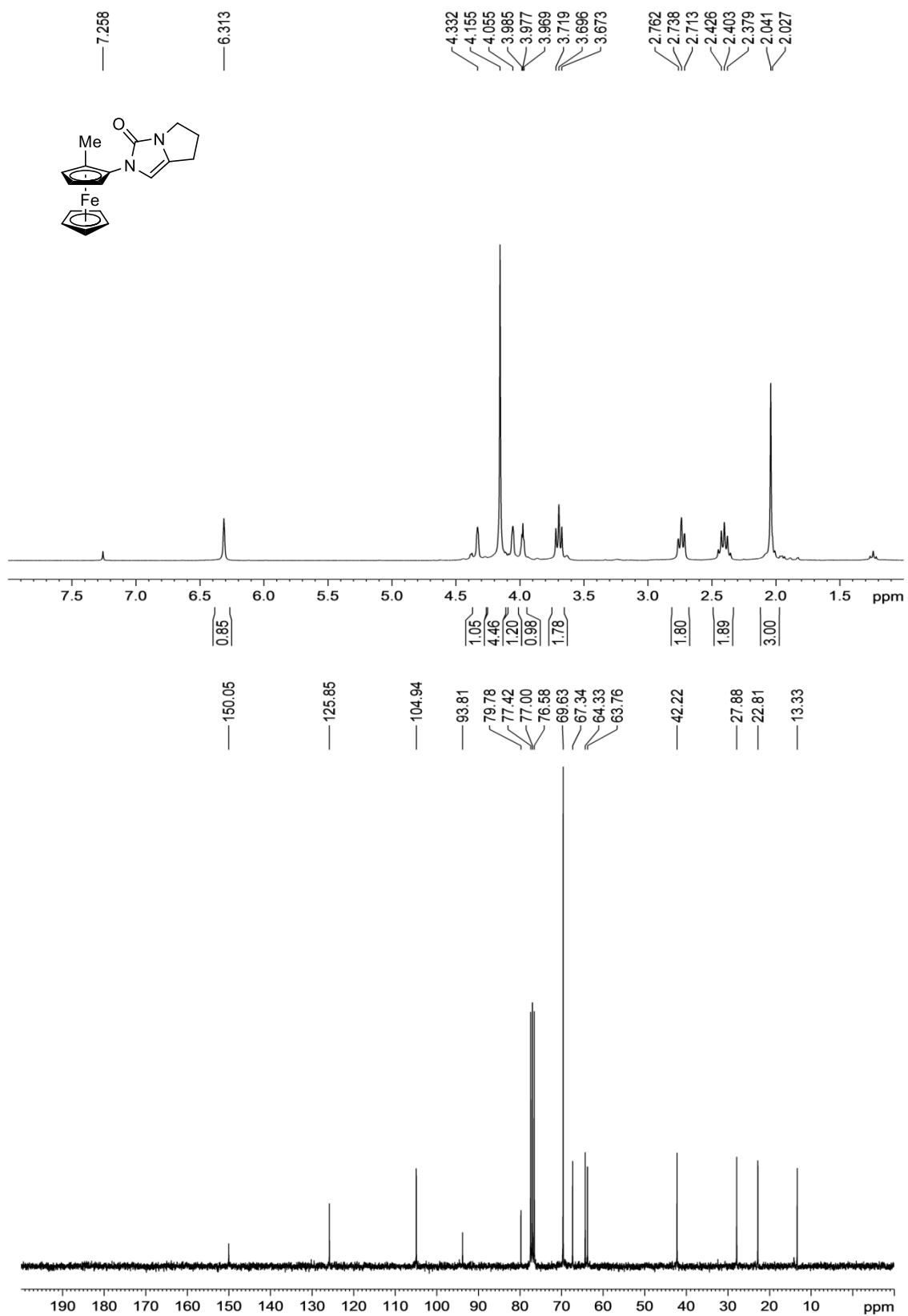
1D proton



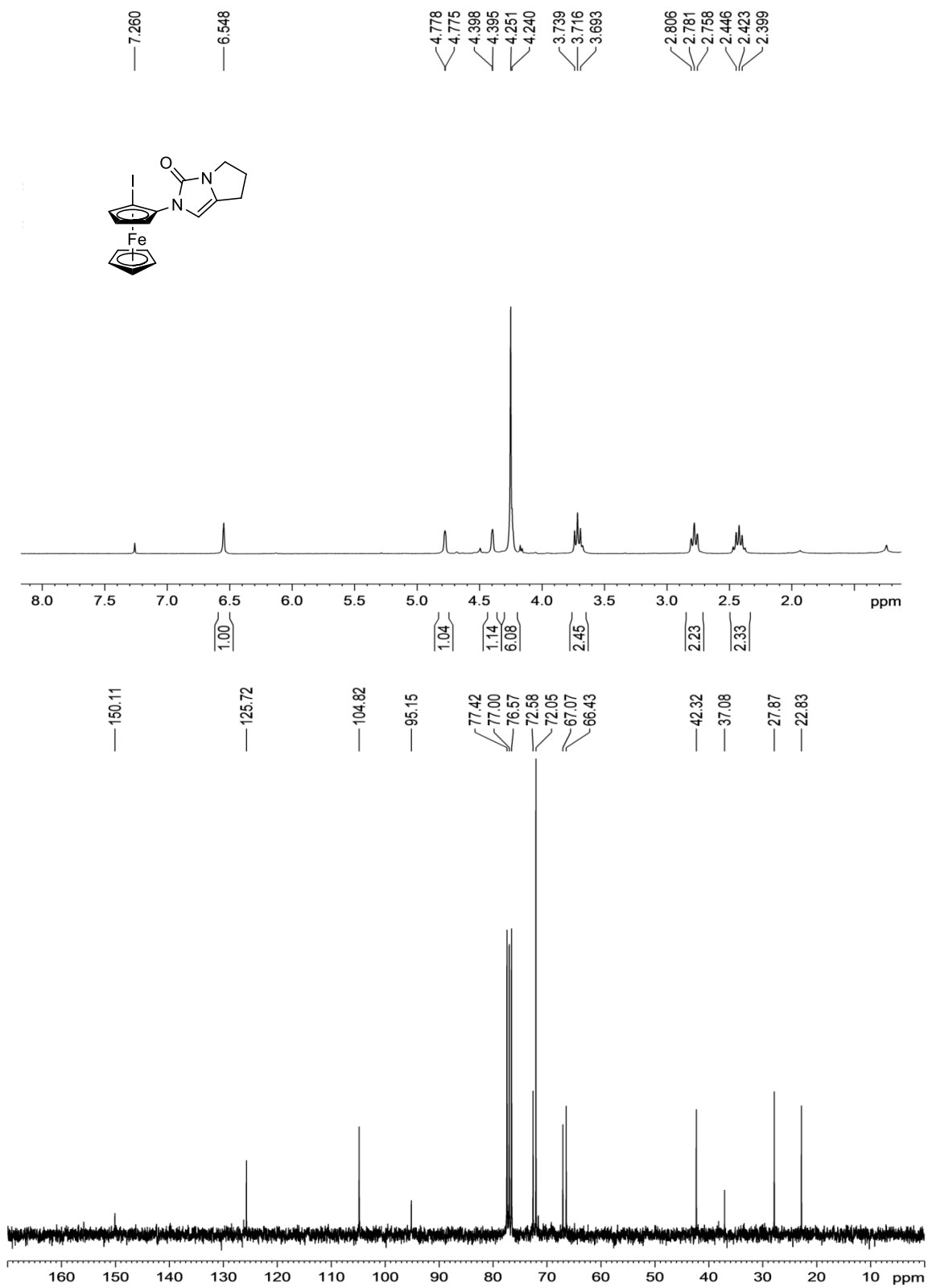
1D carbon with proton decoupling



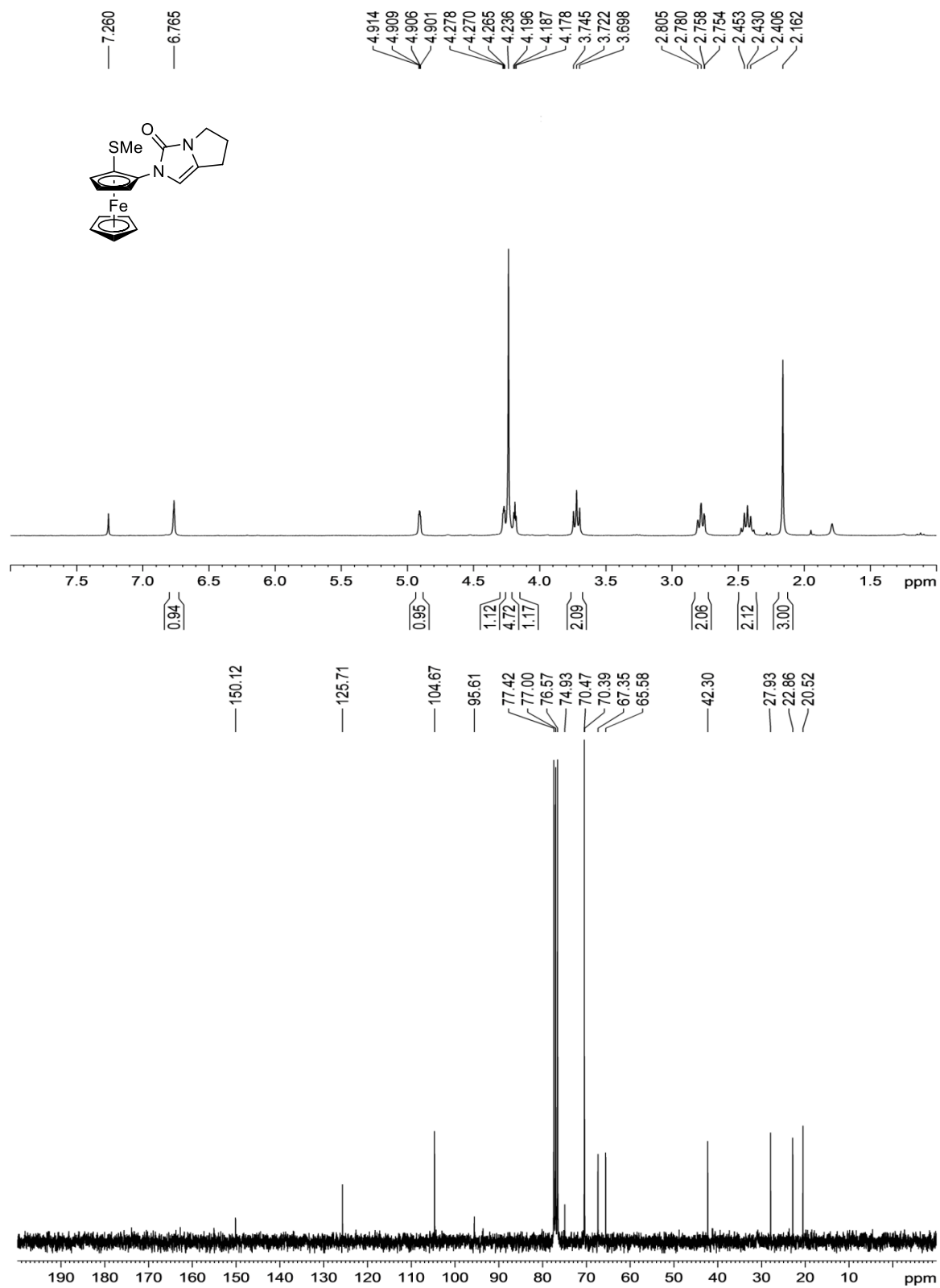
^1H and ^{13}C spectra for unsaturated urea **192a**.



¹H and ¹³C spectra for **192b**.

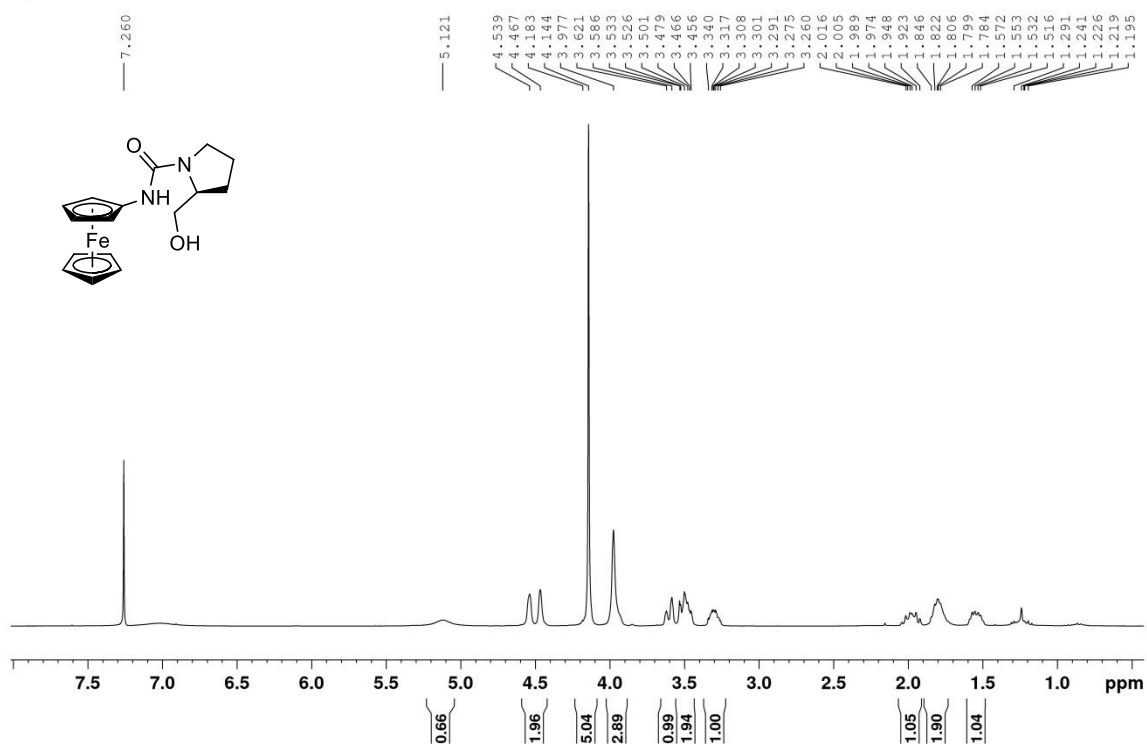


^1H and ^{13}C spectra for **192c**.

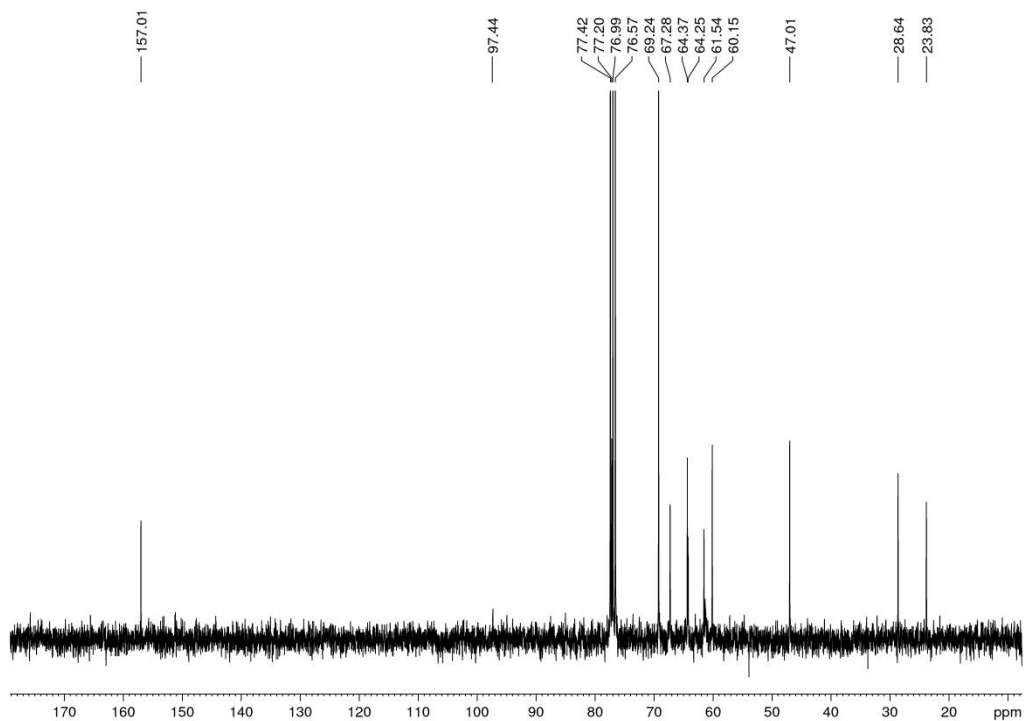


¹H and ¹³C spectra for **192d**.

¹H proton

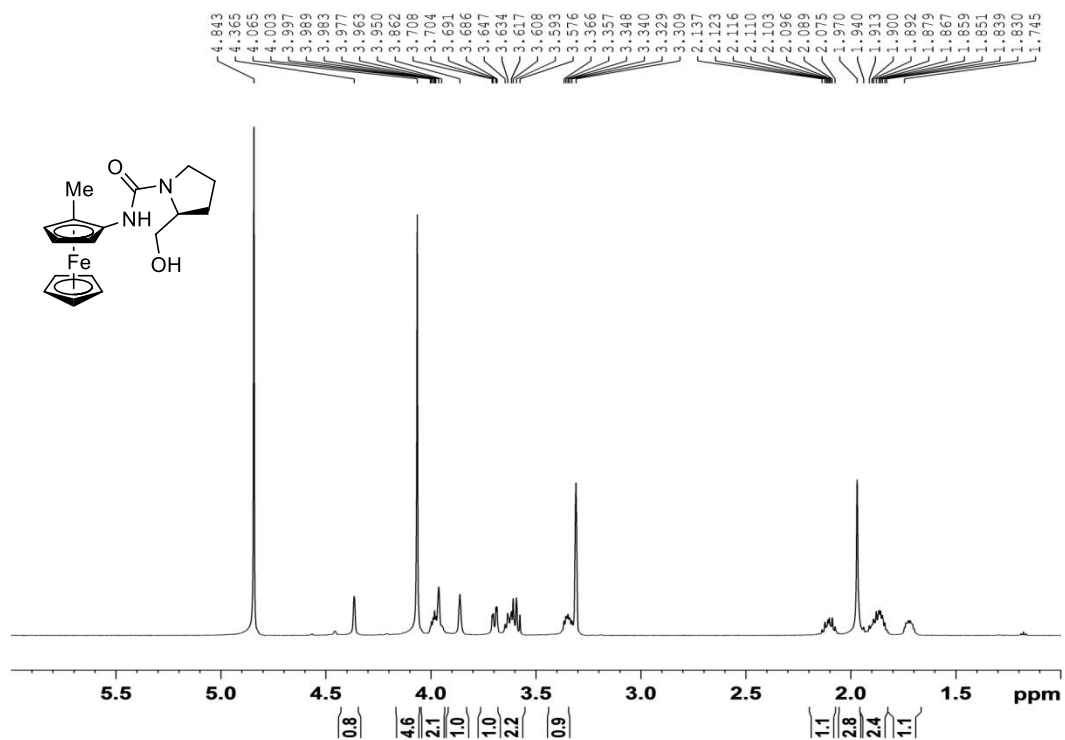


¹D carbon with proton decoupling

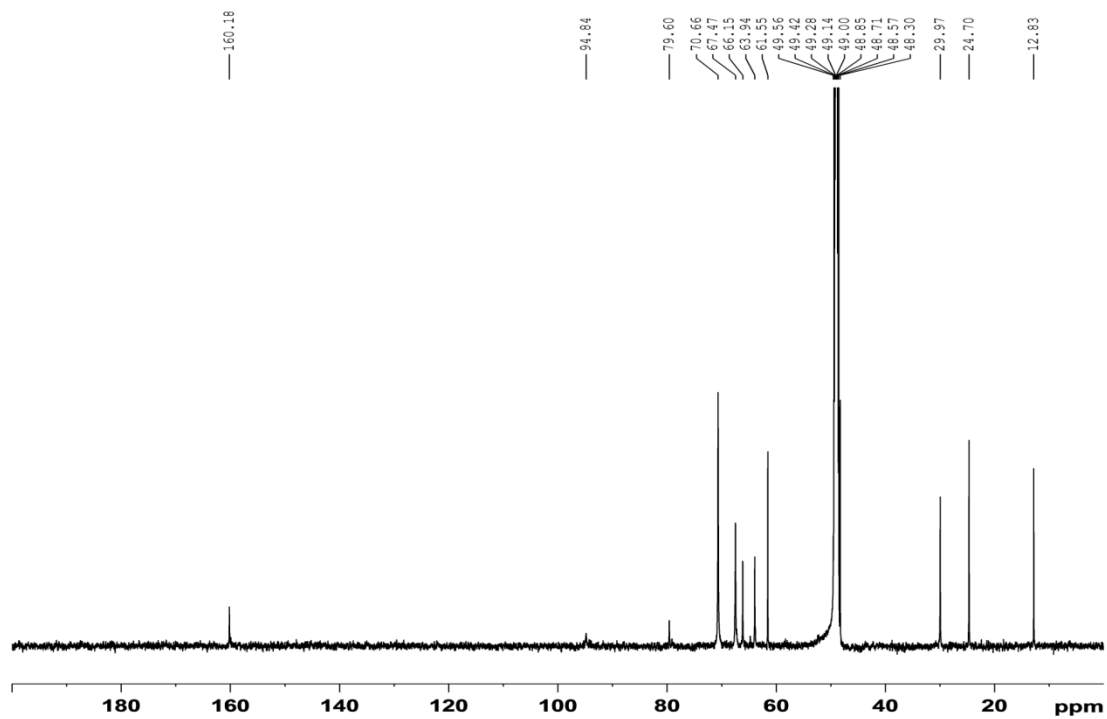


¹H and ¹³C spectra for **191a**.

1d proton

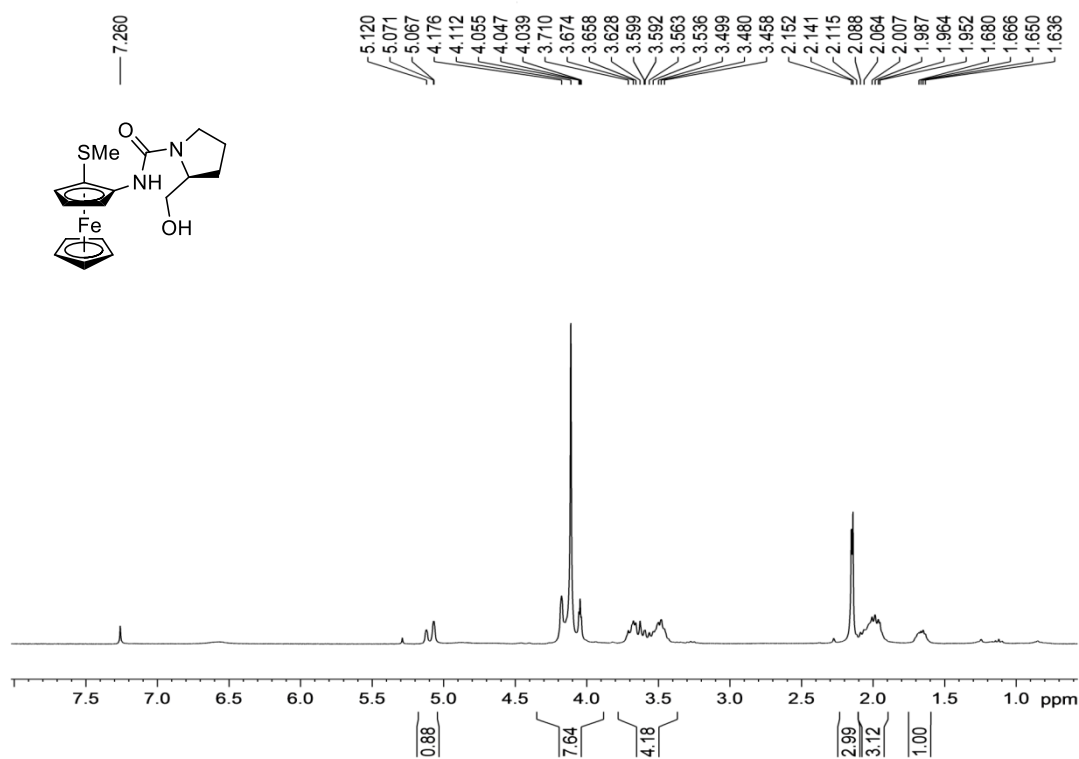


1d carbon with proton decoupling

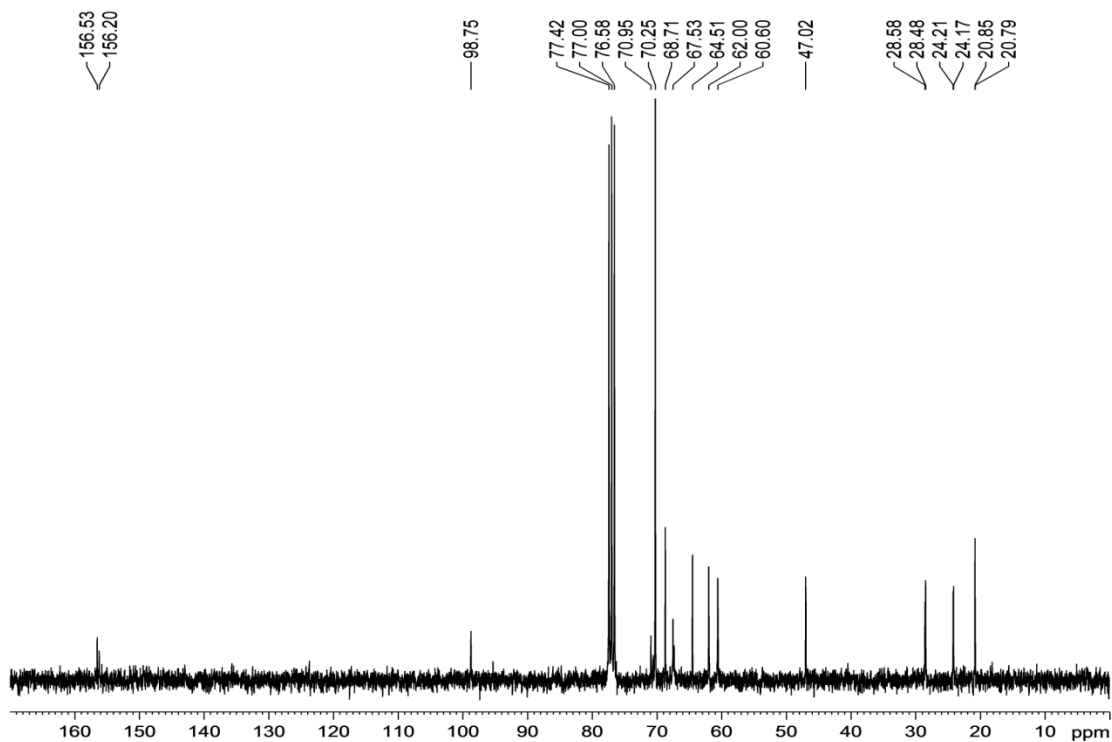


¹H and ¹³C spectra for **191b**.

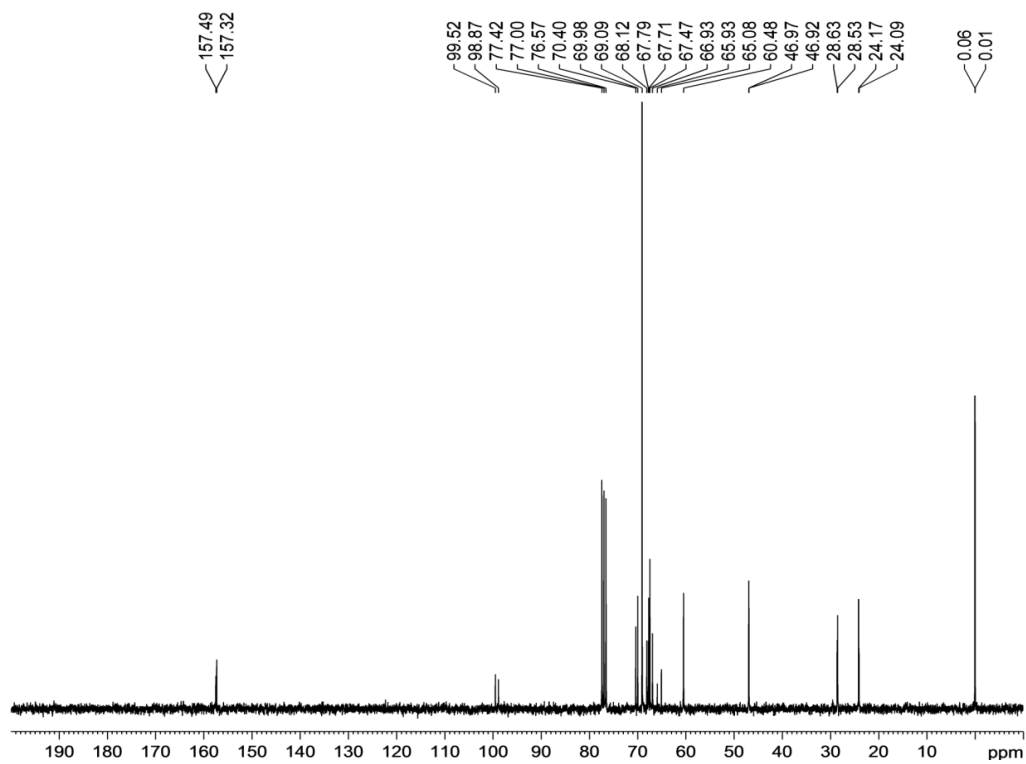
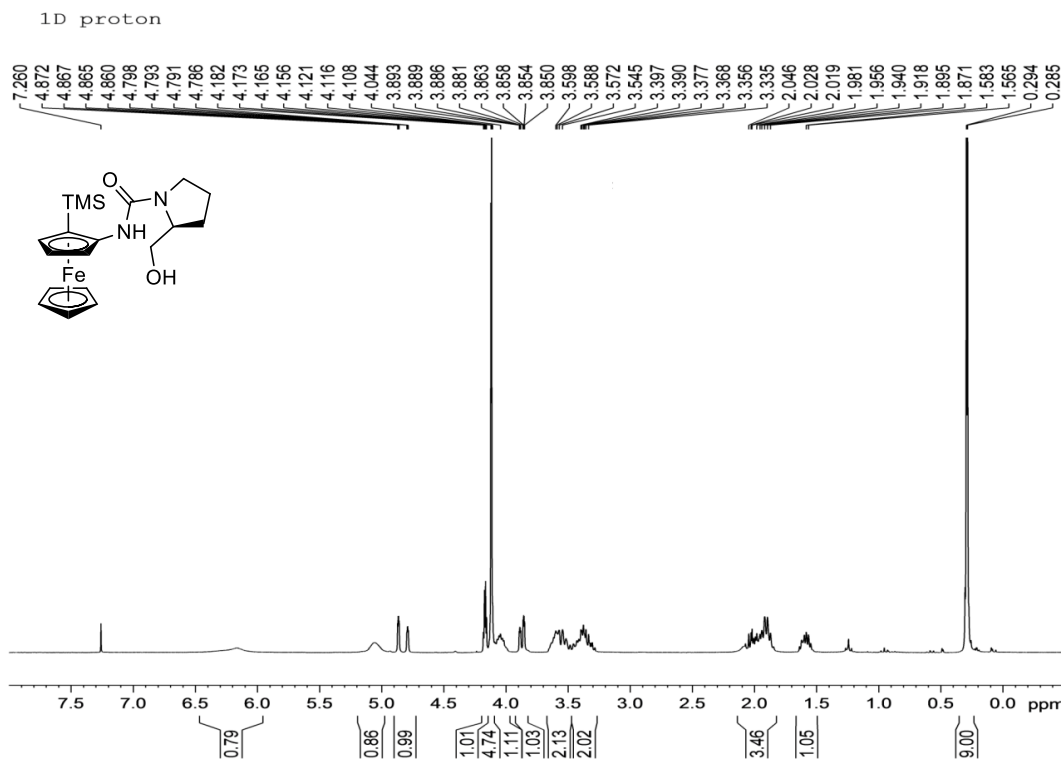
1D proton



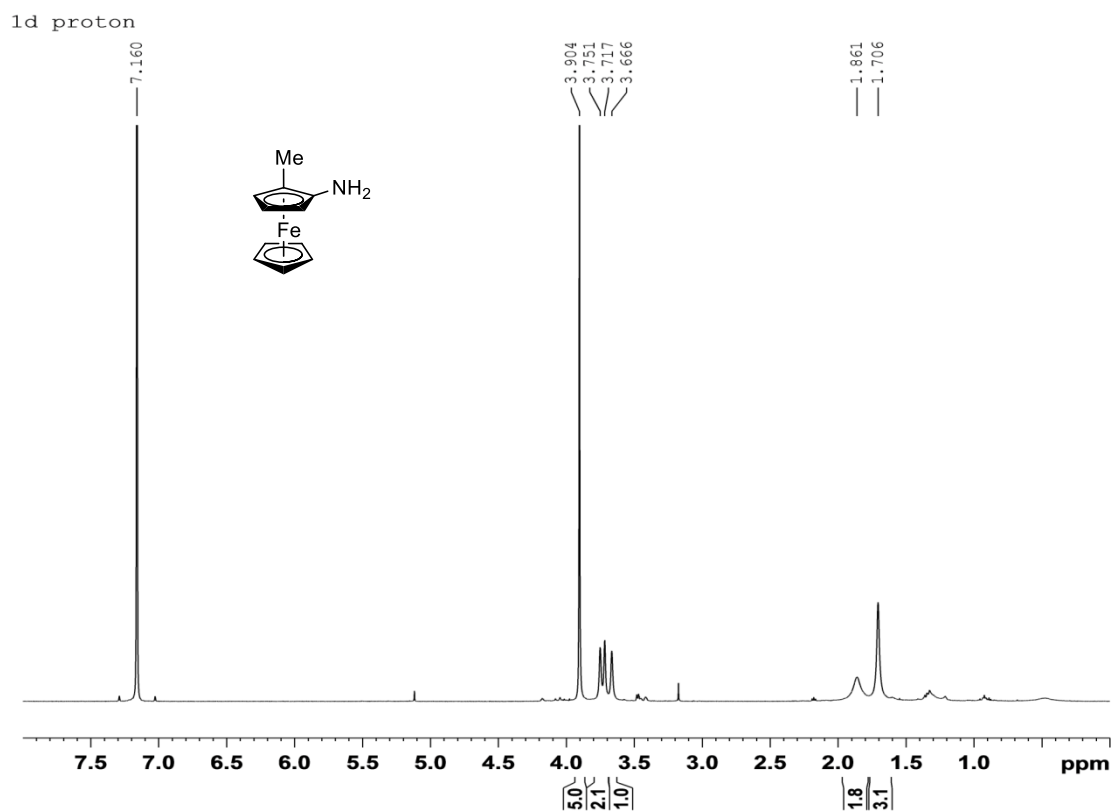
1D carbon with proton decoupling



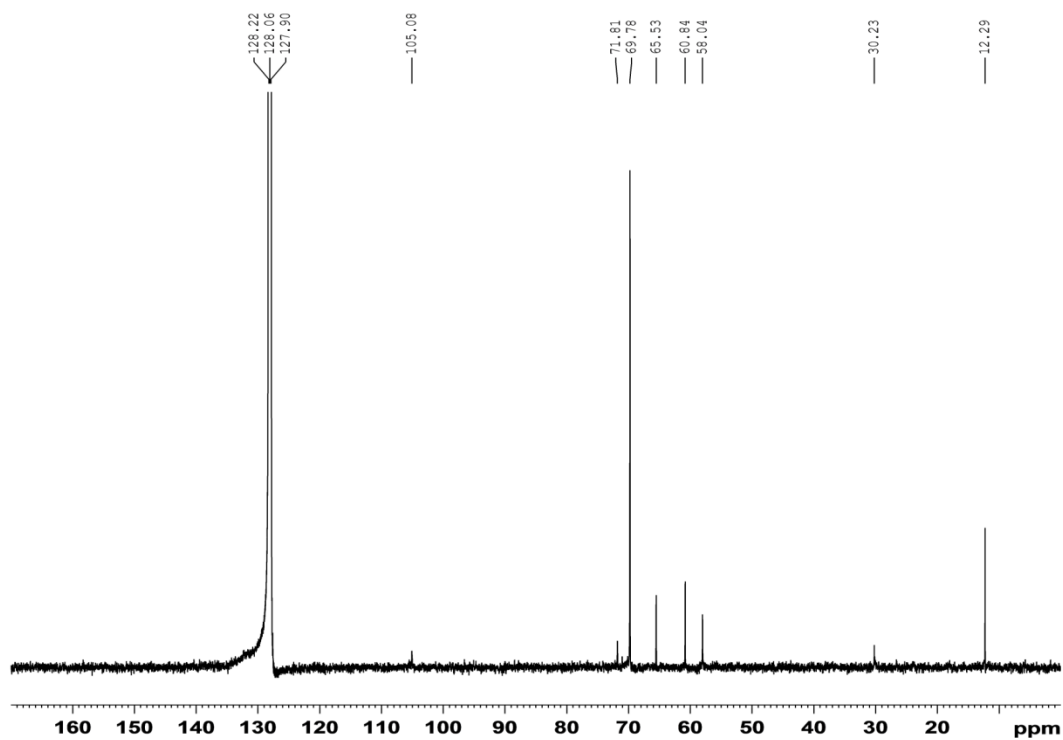
¹H and ¹³C spectra for **191c**.



^1H and ^{13}C spectra for **191d**.

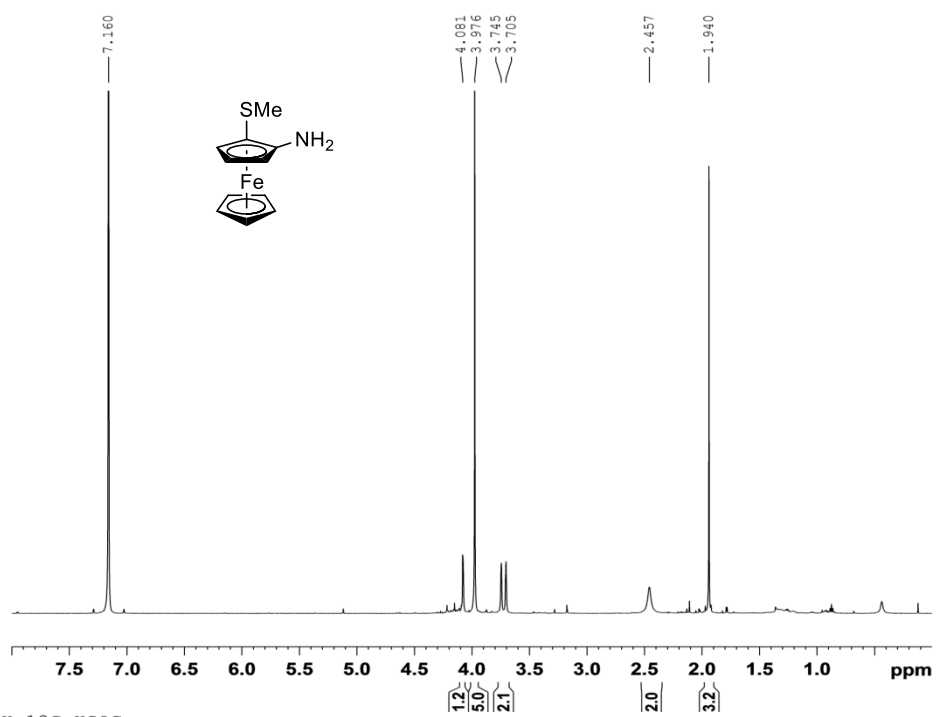


1d carbon with proton decoupling

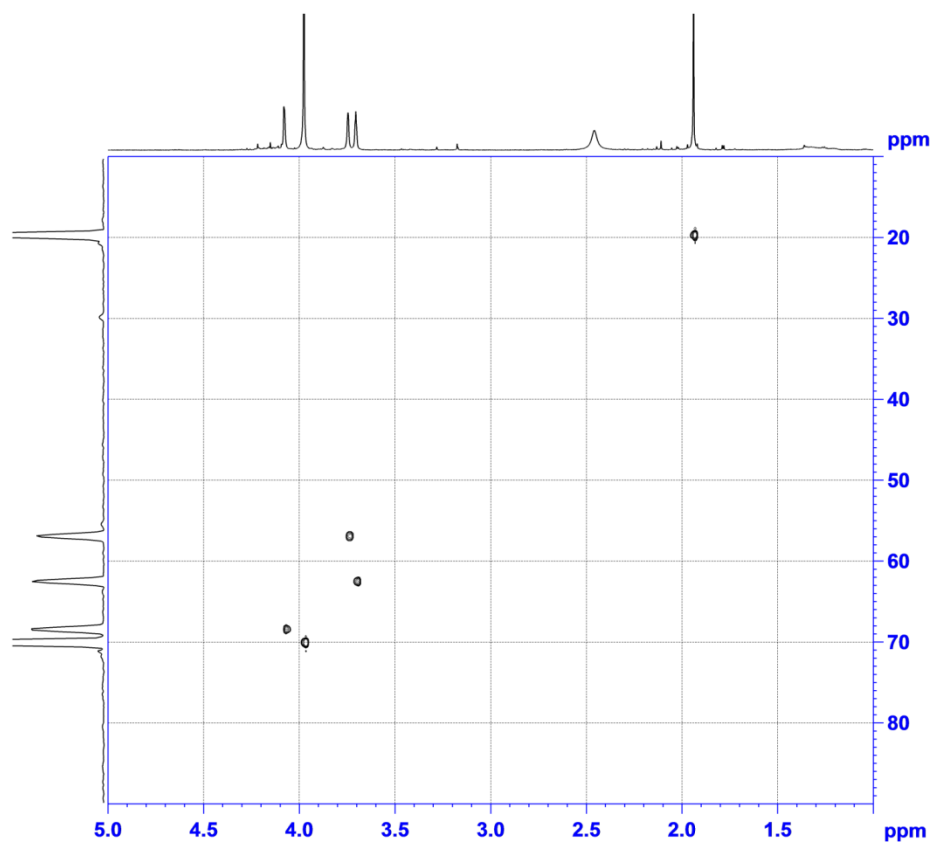


^1H and ^{13}C spectra for **189b**.

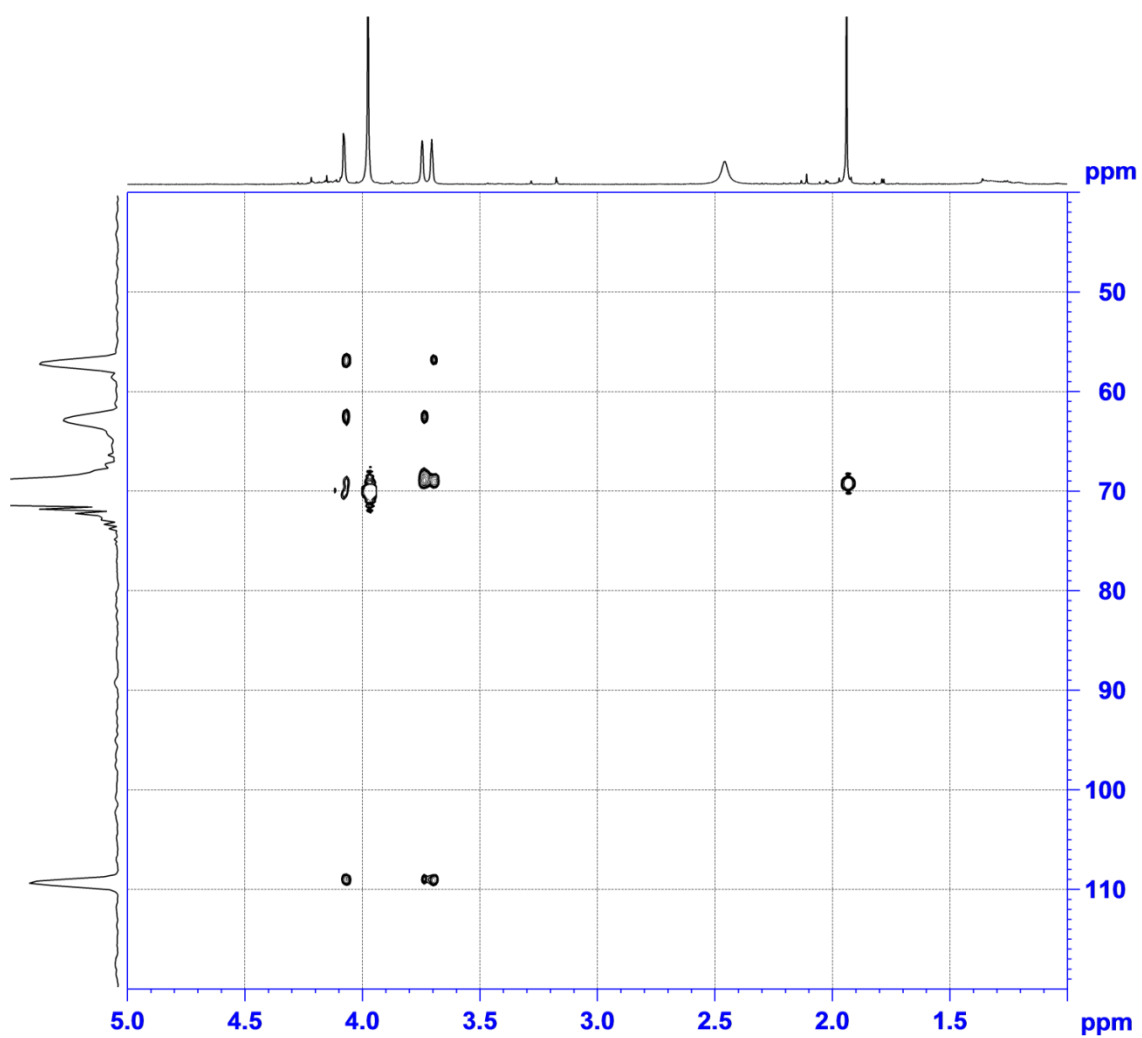
1d proton



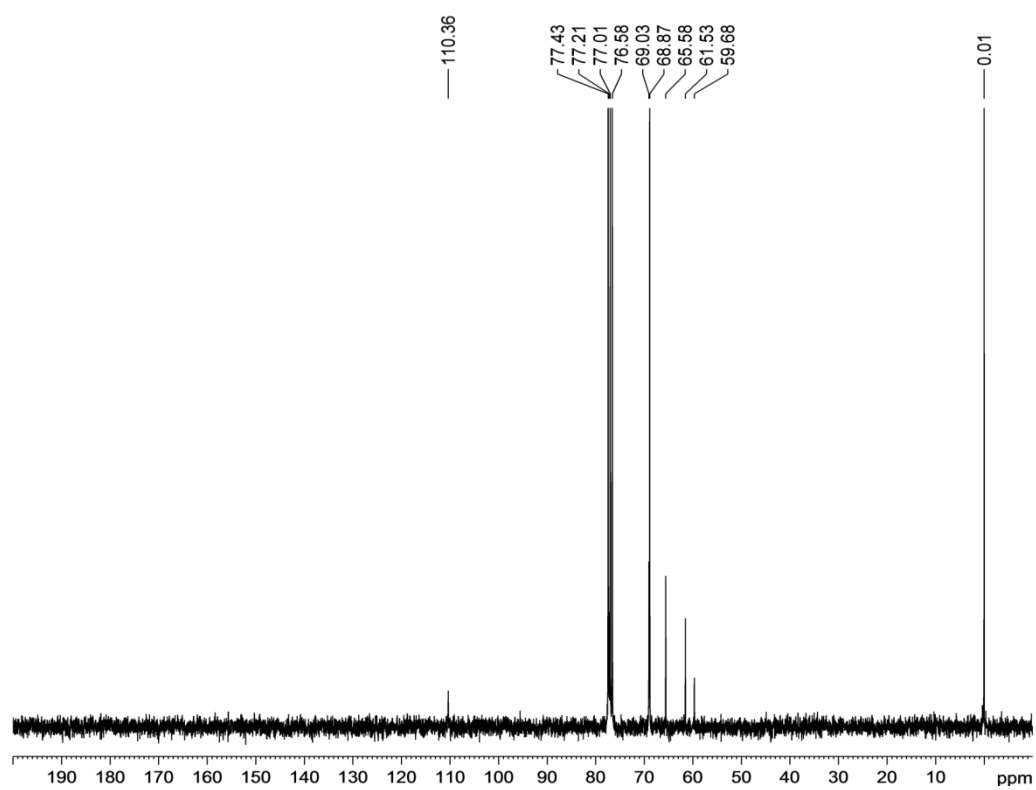
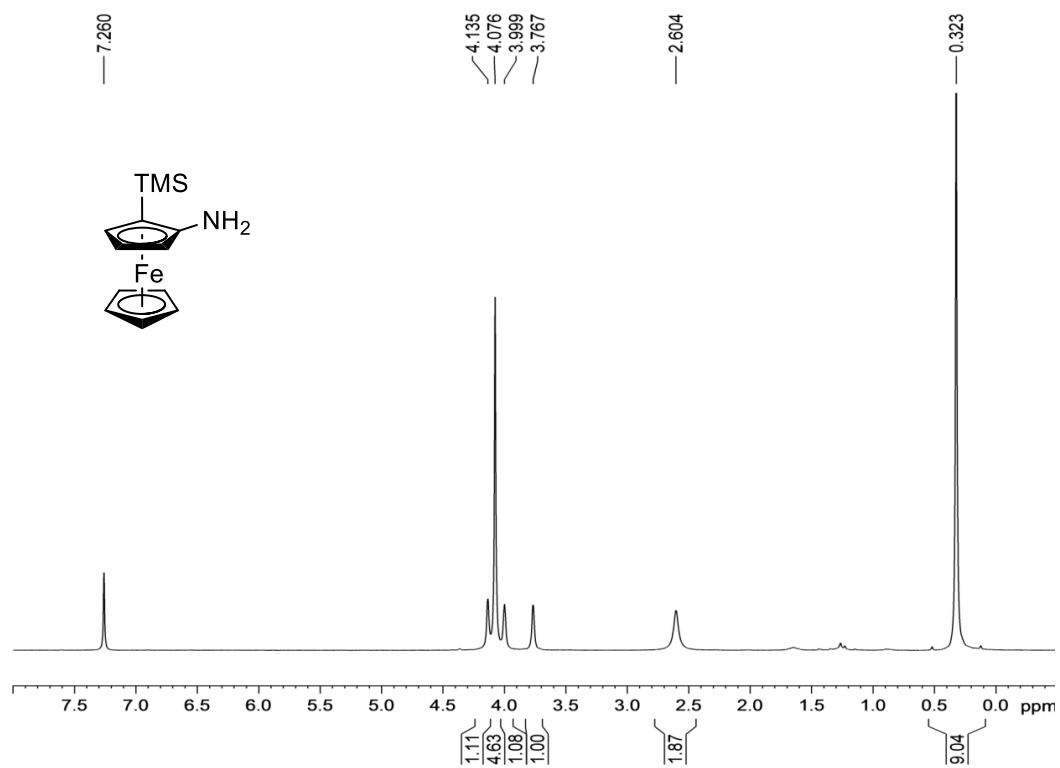
H-13C HSQC



HMBC

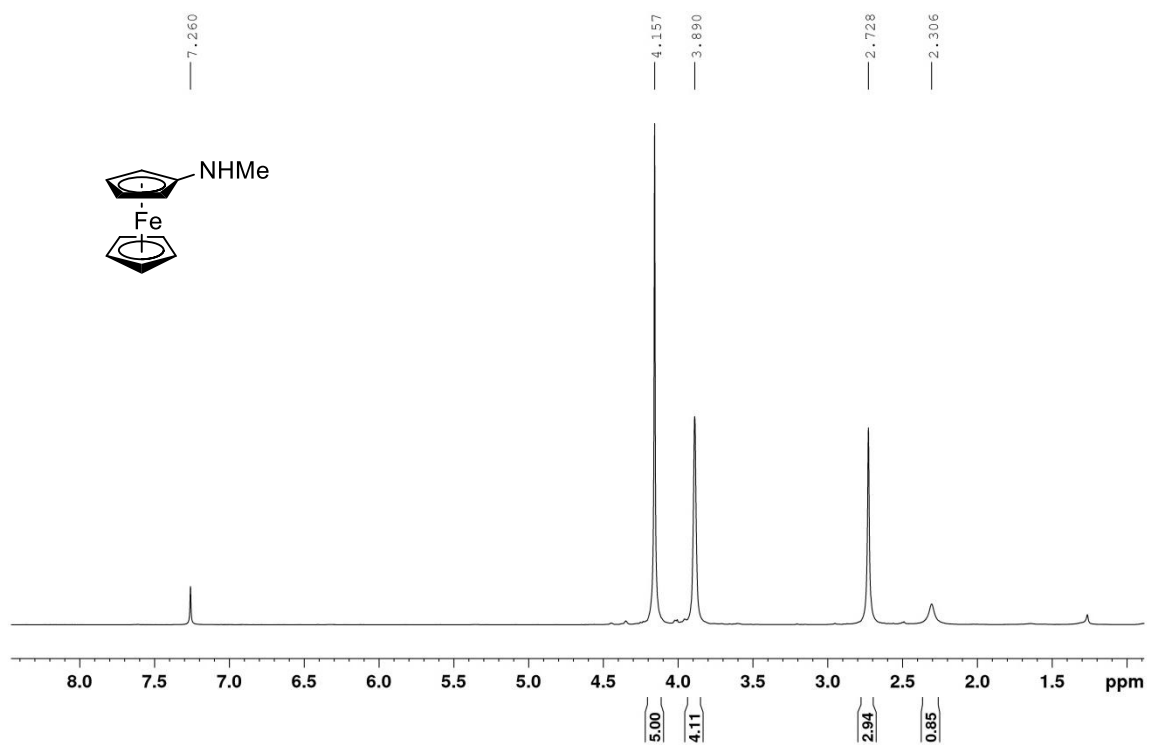


^1H and HSQC and HMBC spectra for **189c**.

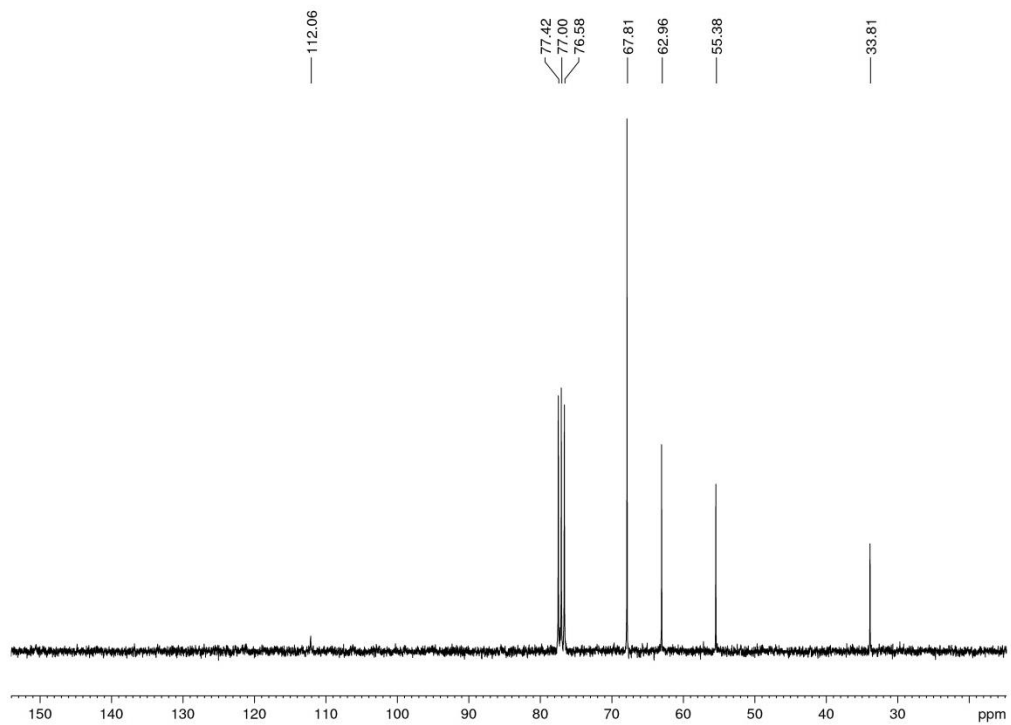


¹H and ¹³C spectra for **189d**.

1D proton

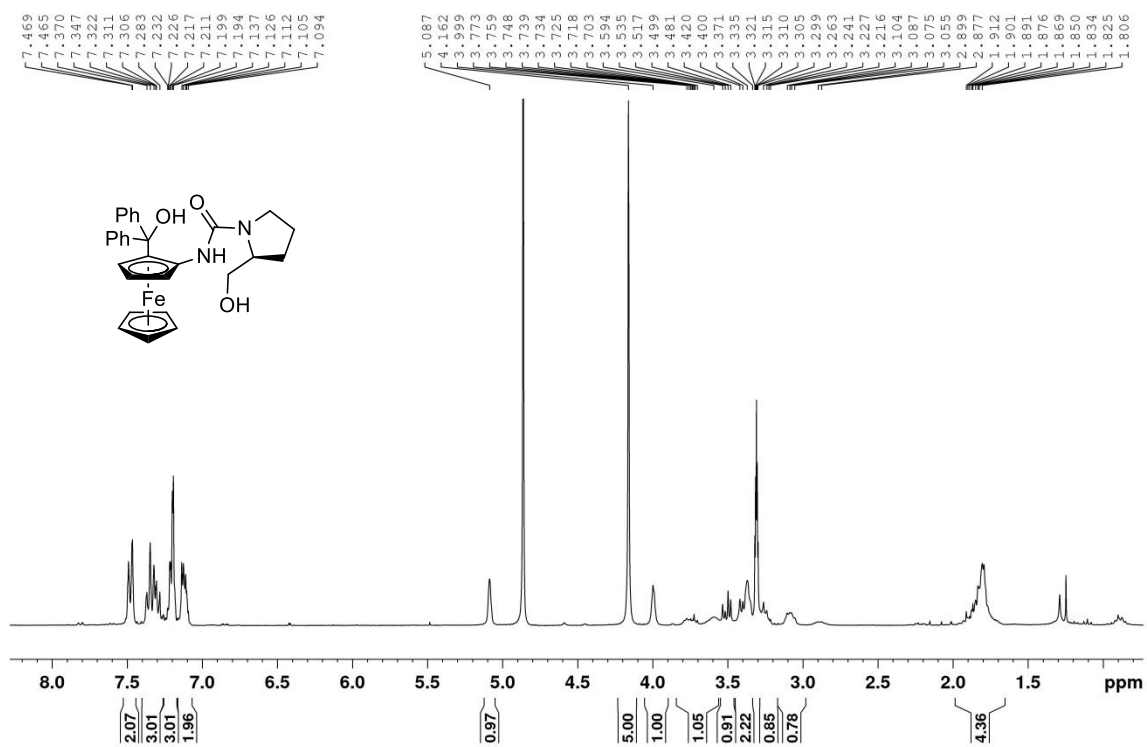


1D carbon with proton decoupling

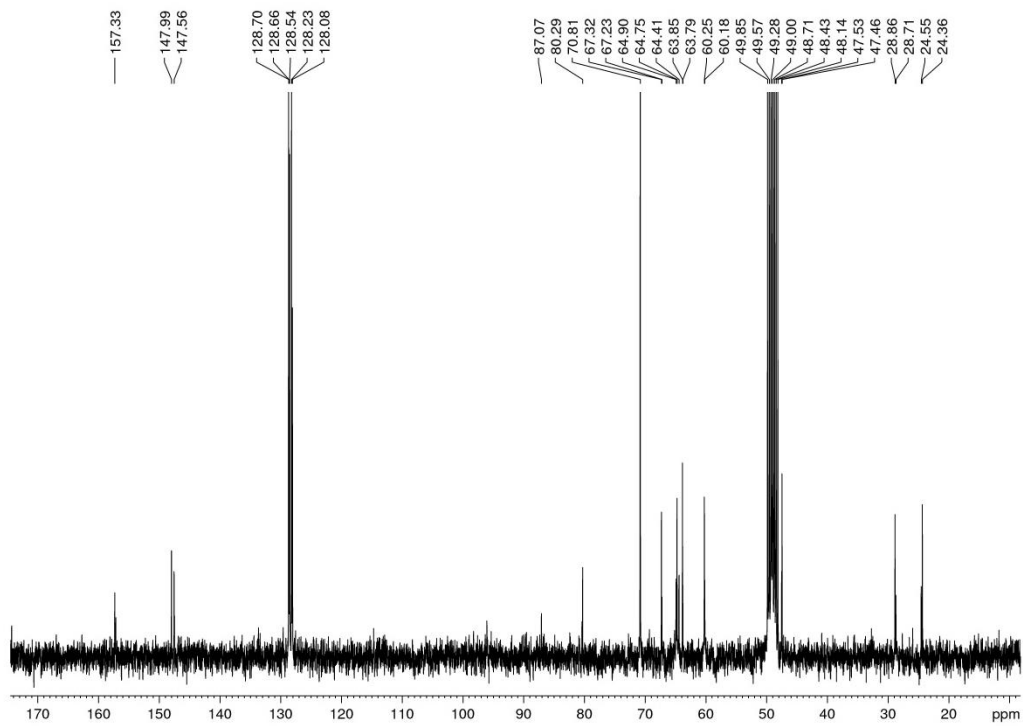


^1H and ^{13}C spectra for **189e**.

D proton

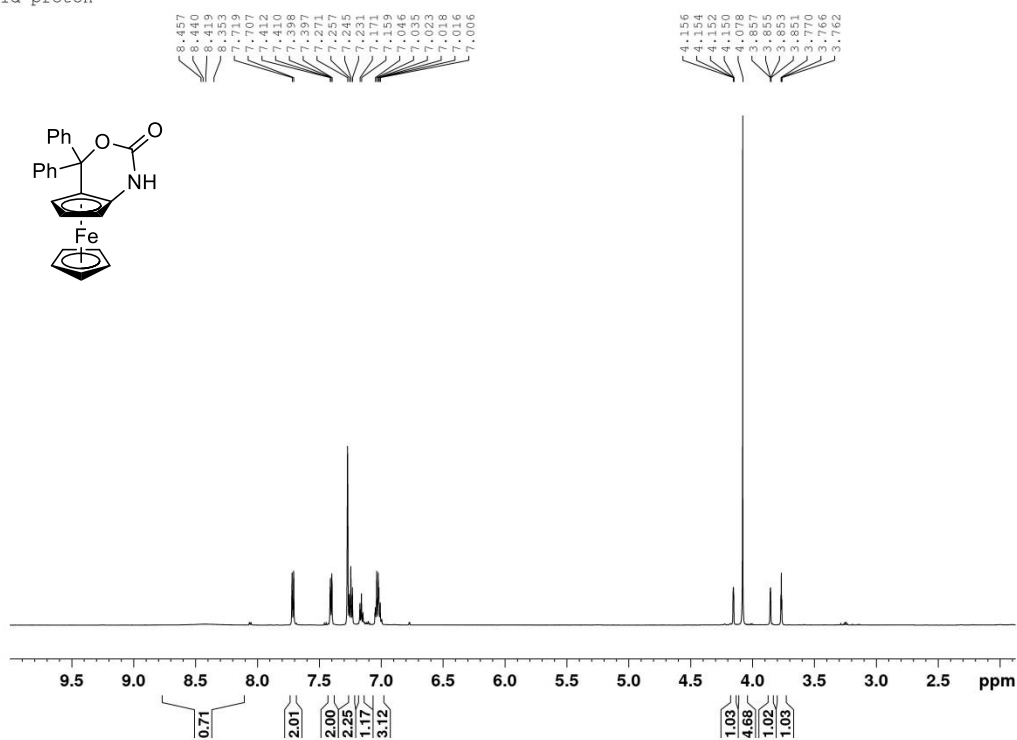


1D carbon with proton decoupling

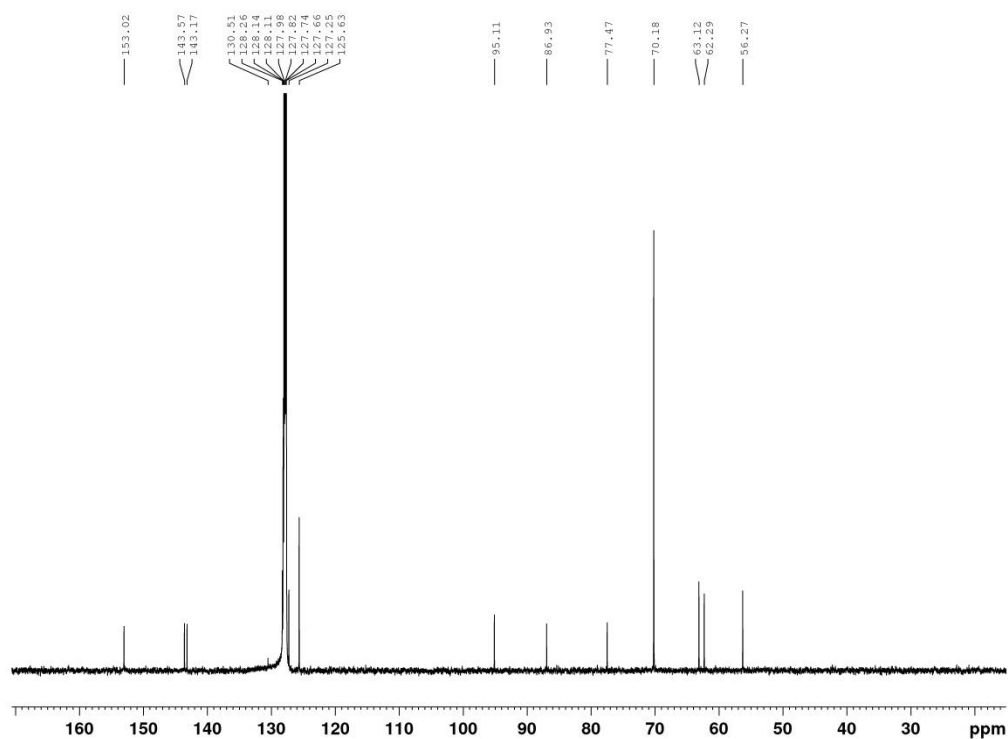


¹H and ¹³C spectra for **191e**.

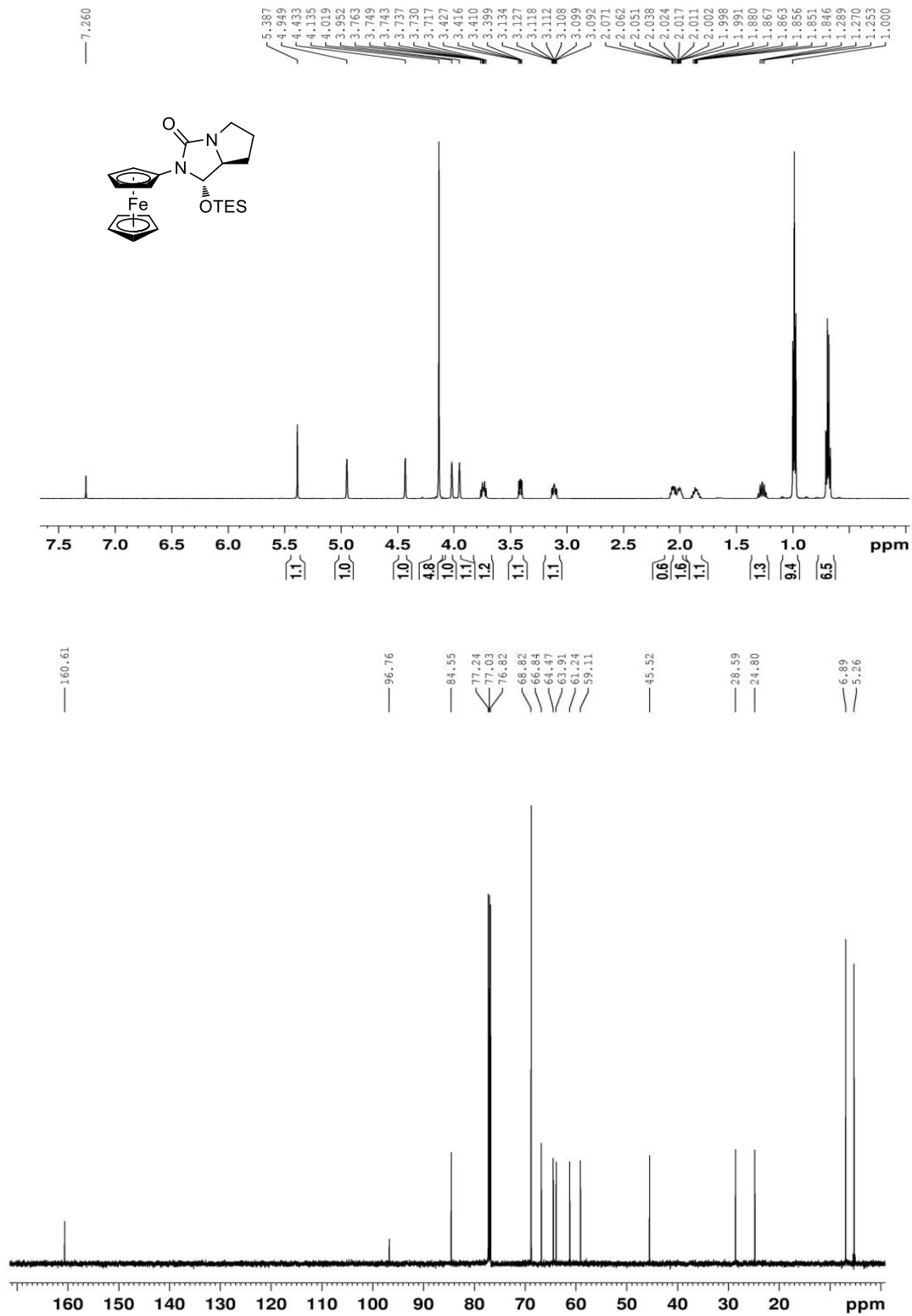
1d proton

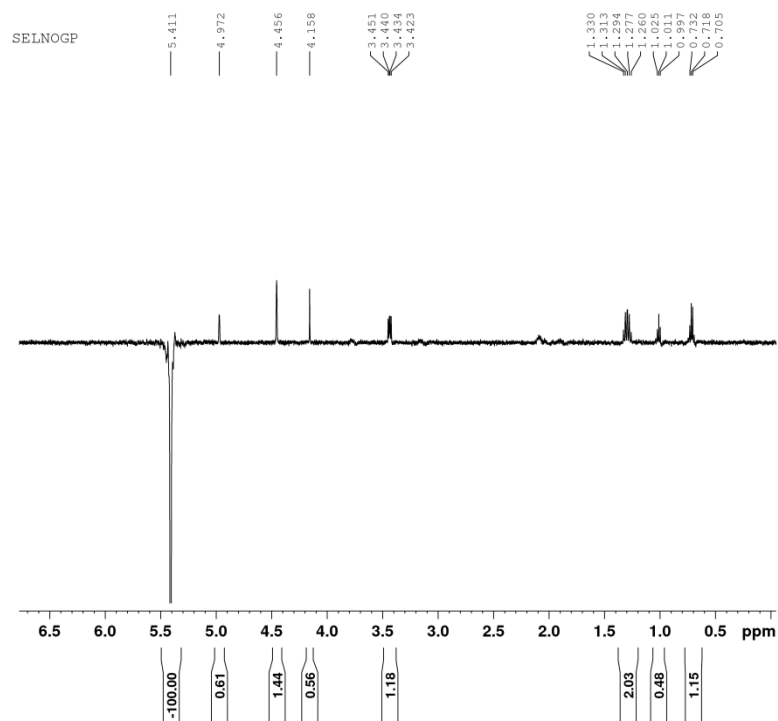


1d carbon with proton decoupling

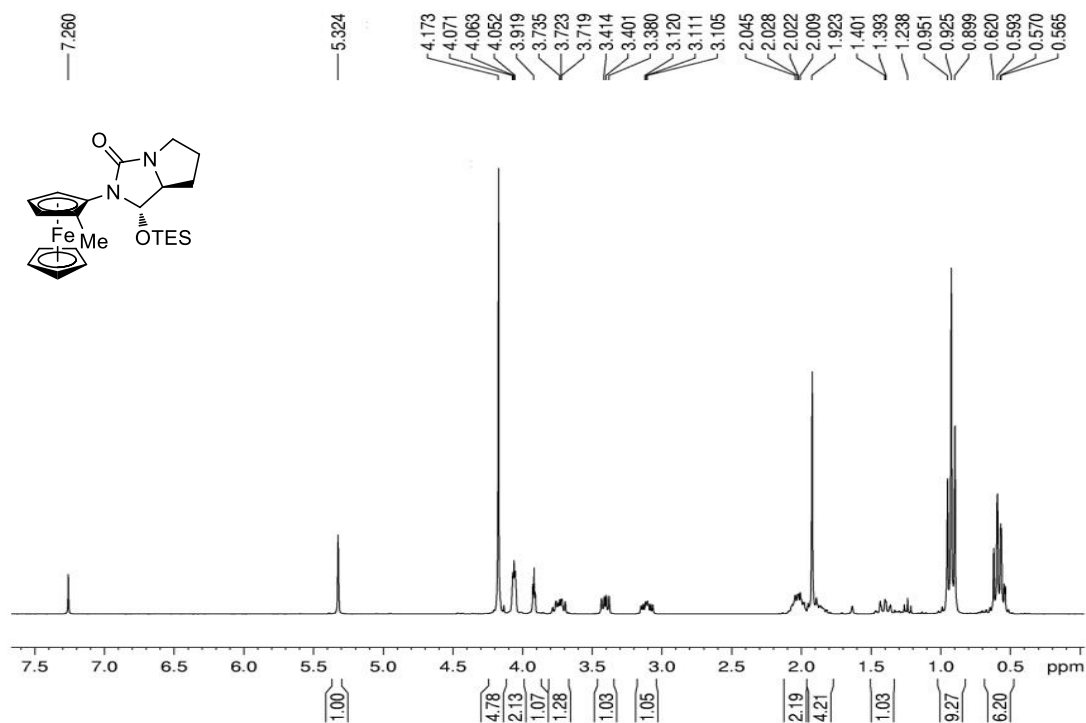


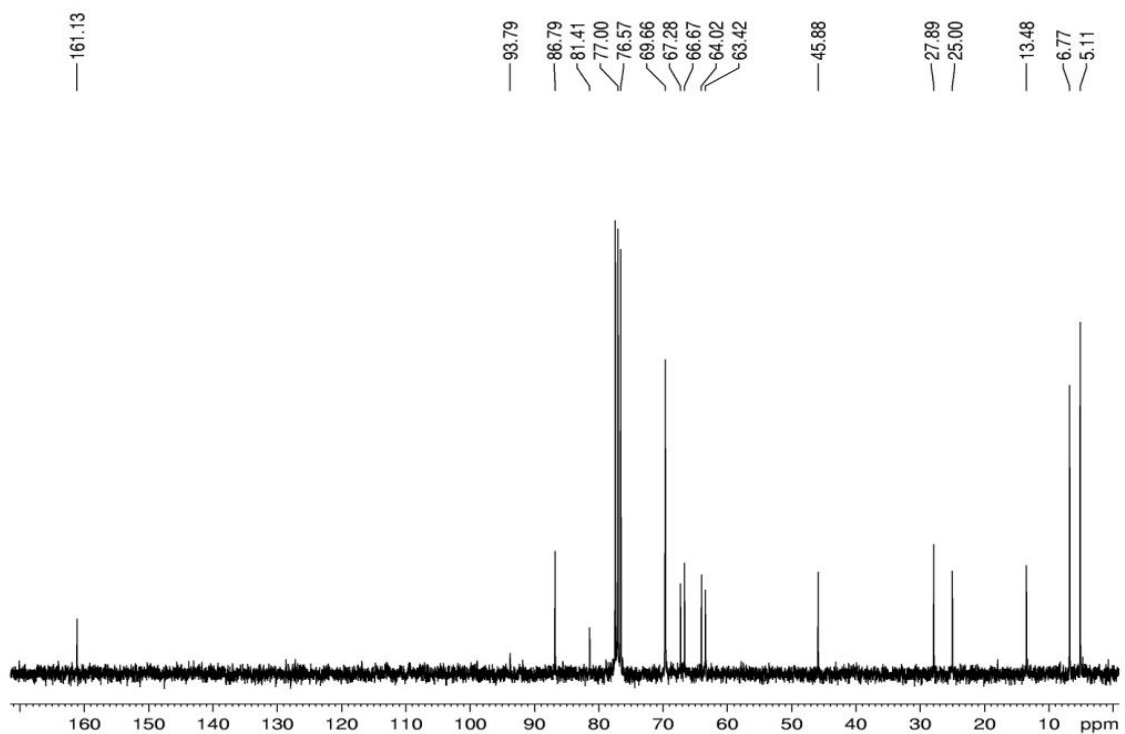
¹H and ¹³C spectra for **193**.



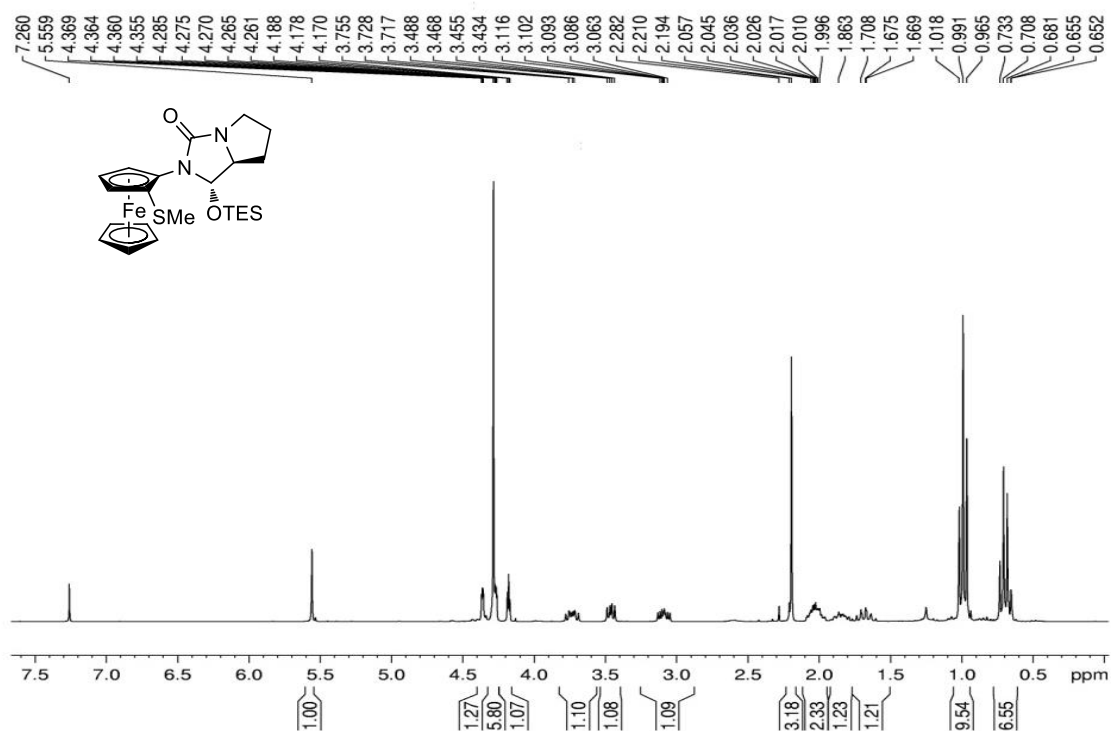


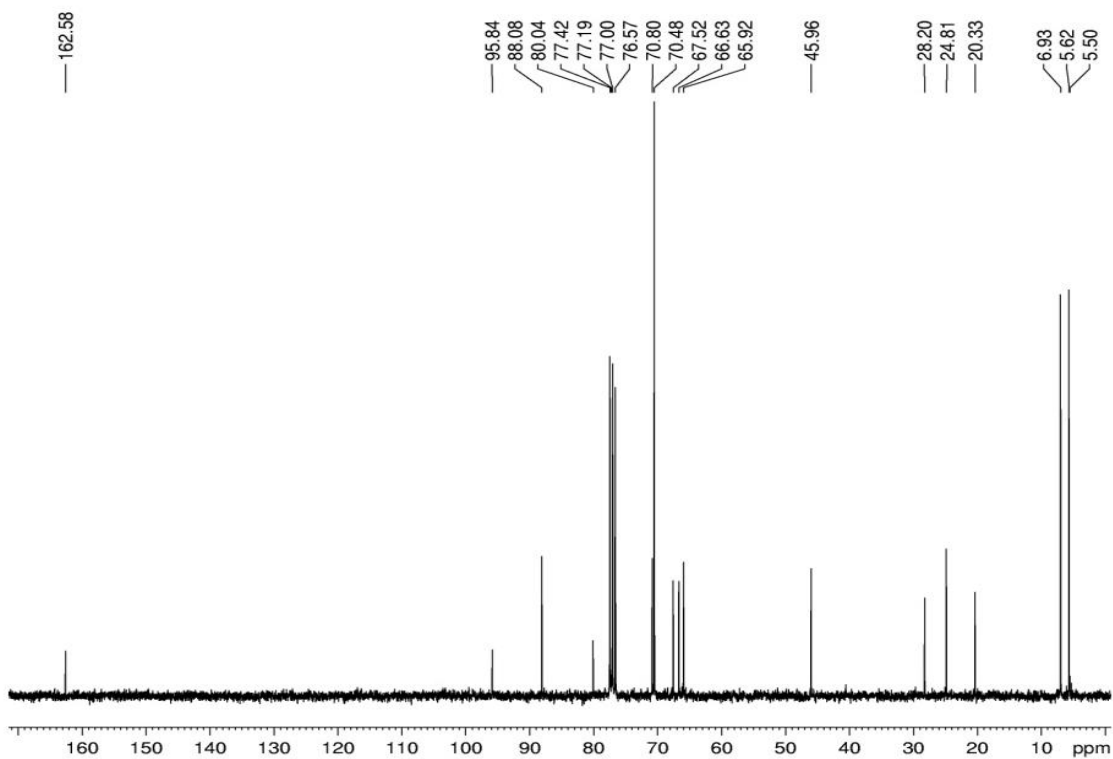
^1H , ^{13}C and nOe spectra for *anti*-**187**.



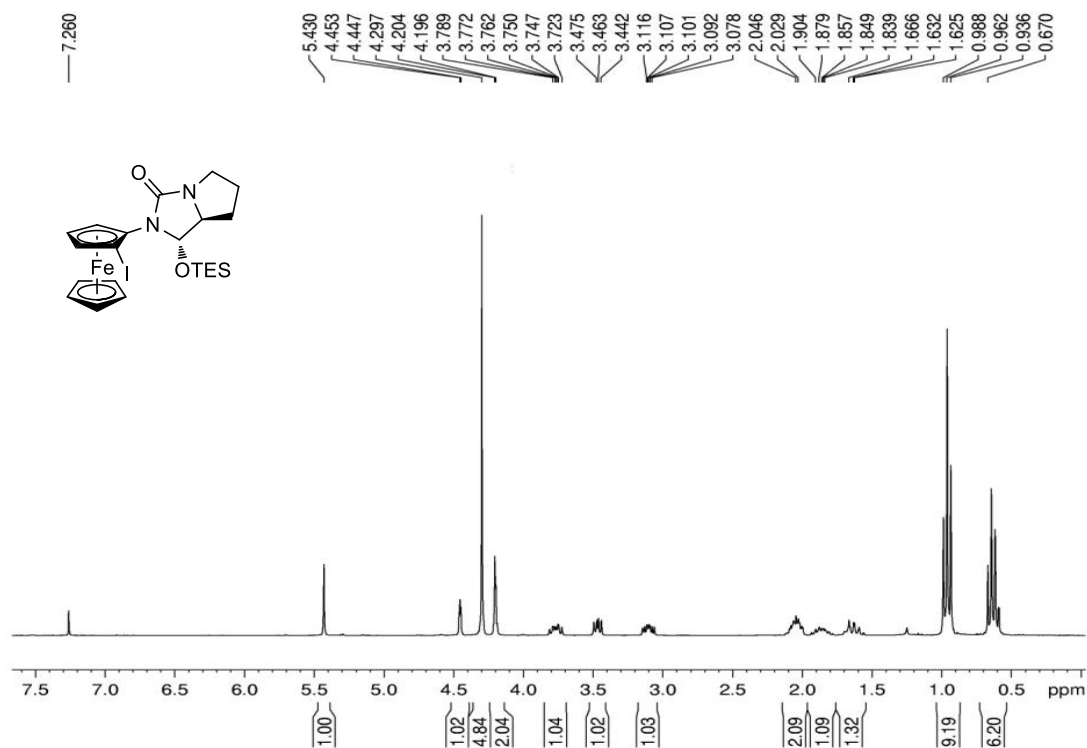


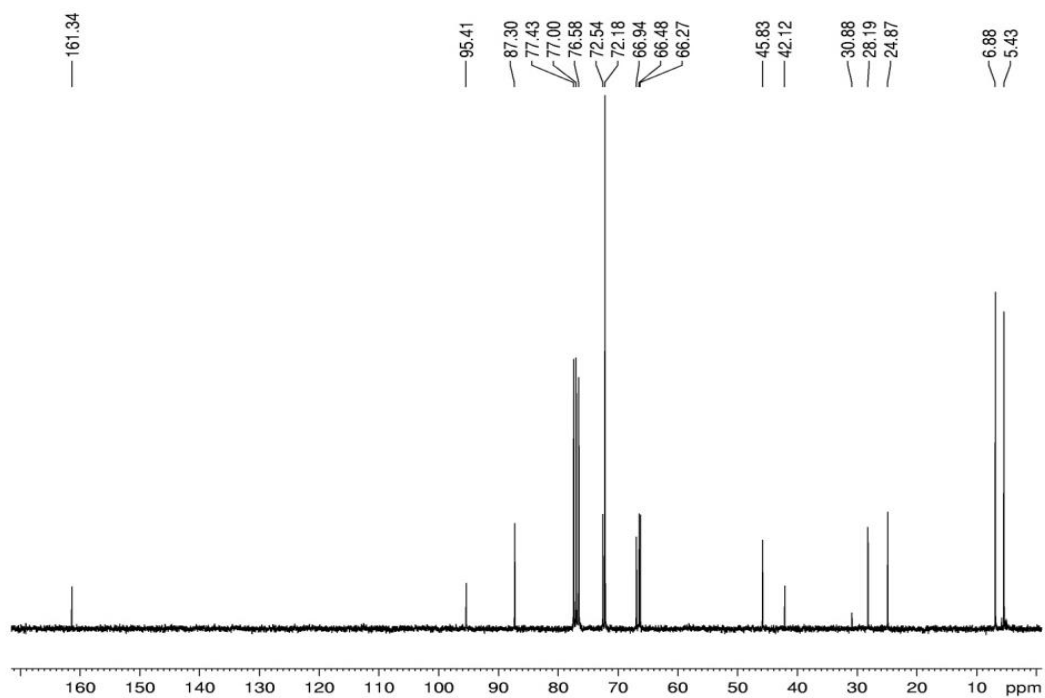
^1H and ^{13}C spectra for **190a**.



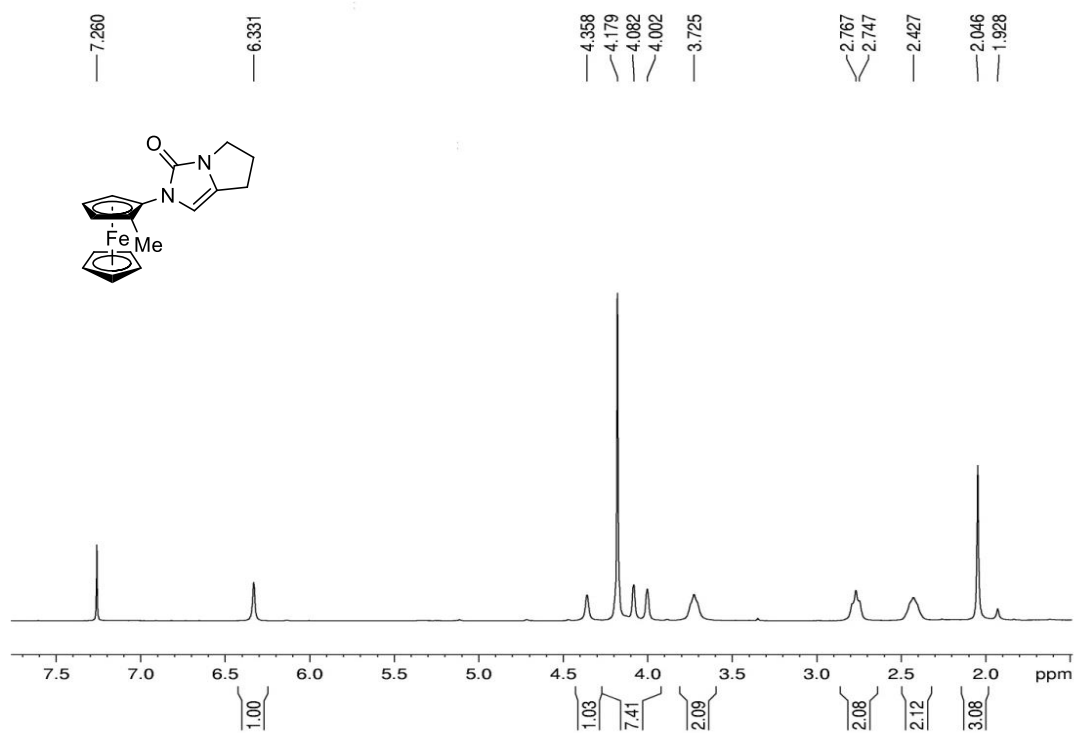


^1H and ^{13}C spectra for **190b**.



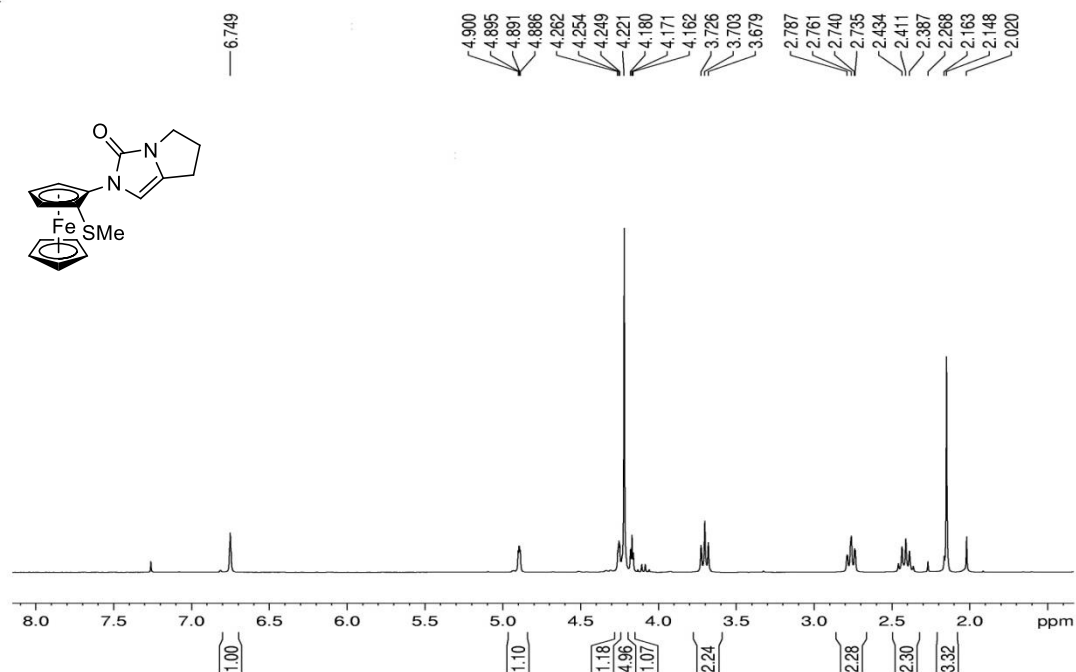


^1H and ^{13}C spectra for **190c**.



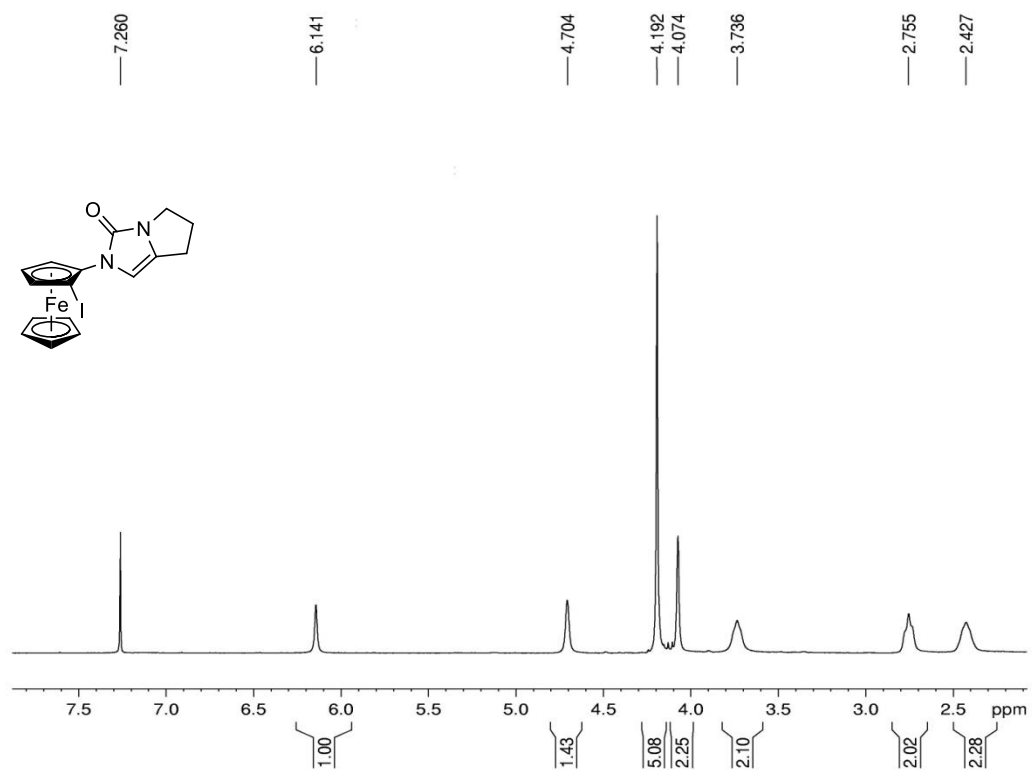
^1H spectrum for *ent*-**192a**.

on

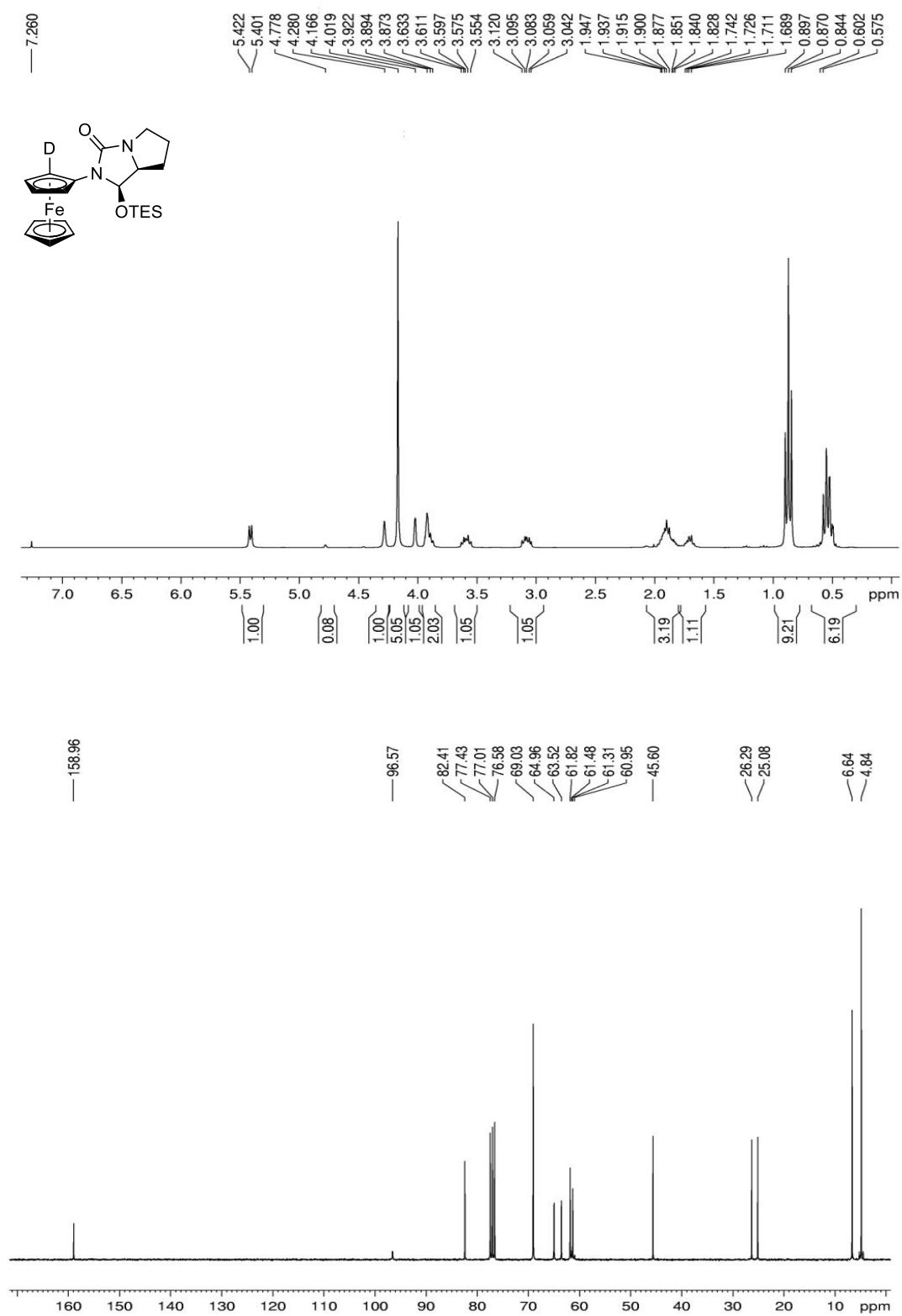


¹H spectrum for *ent*-192b.

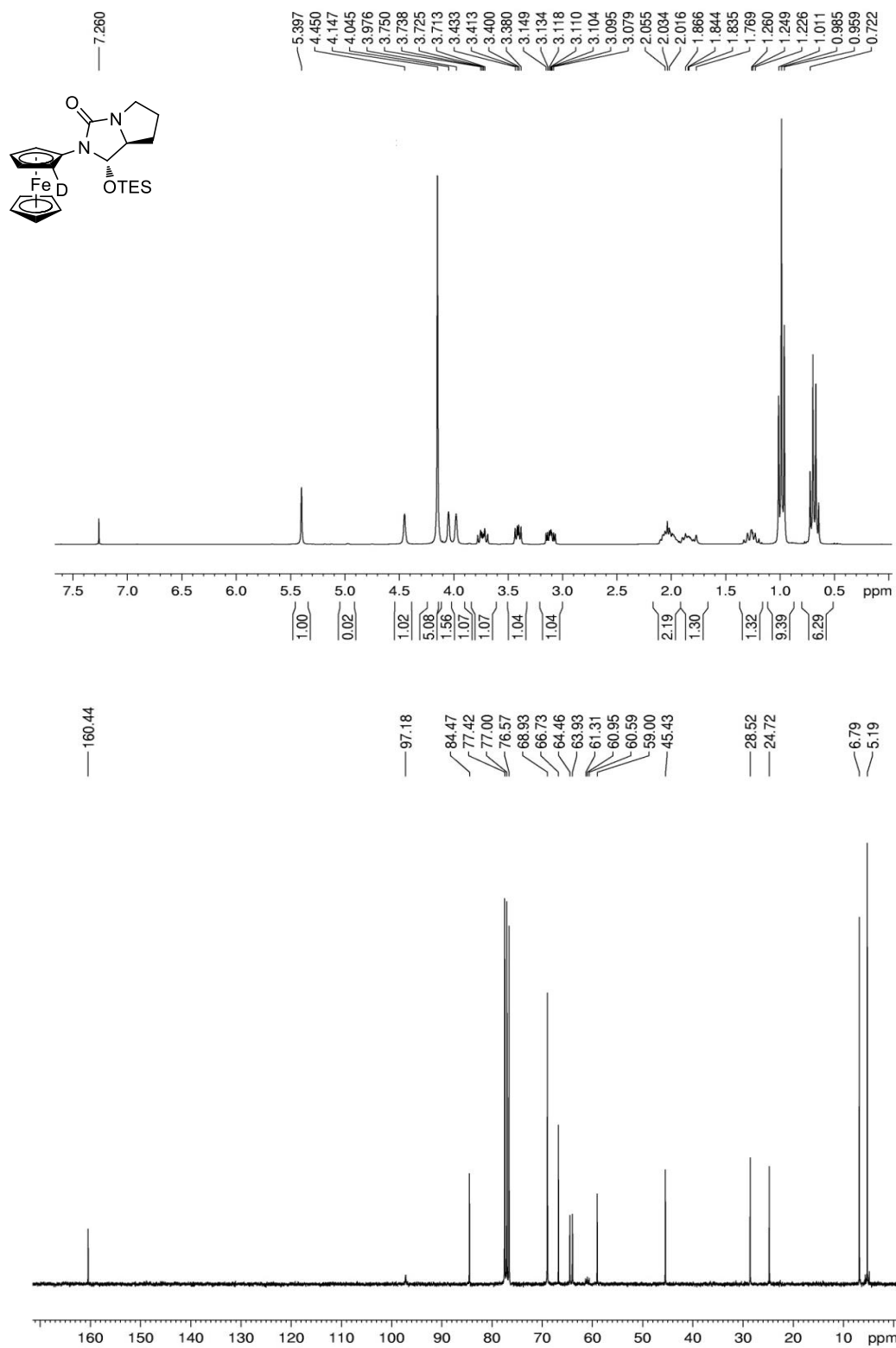
1D proton



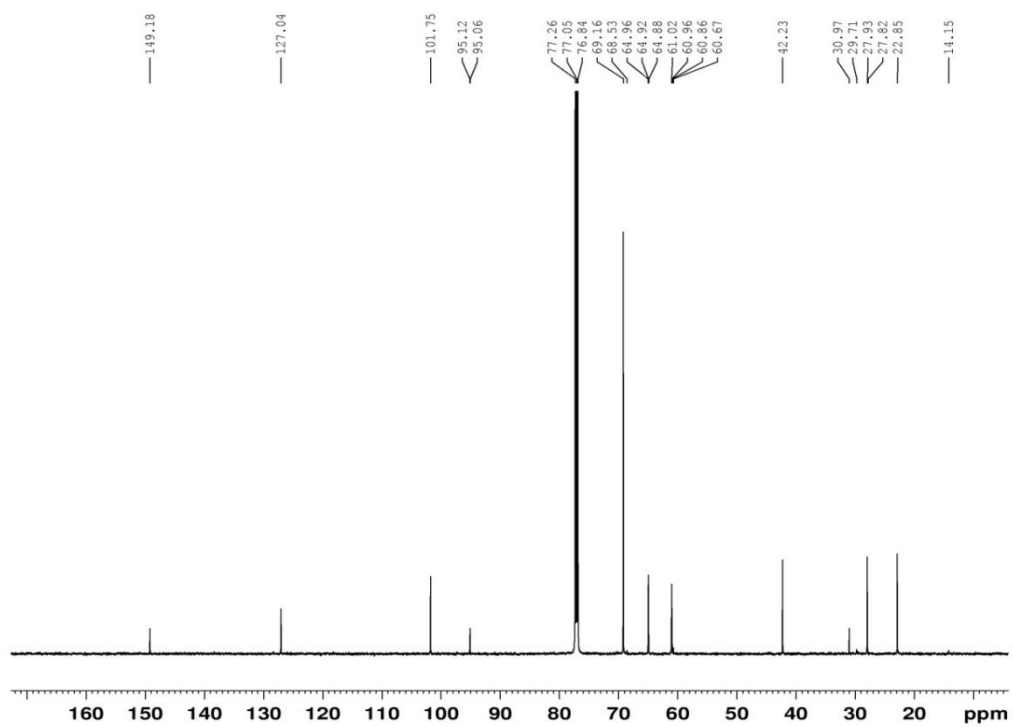
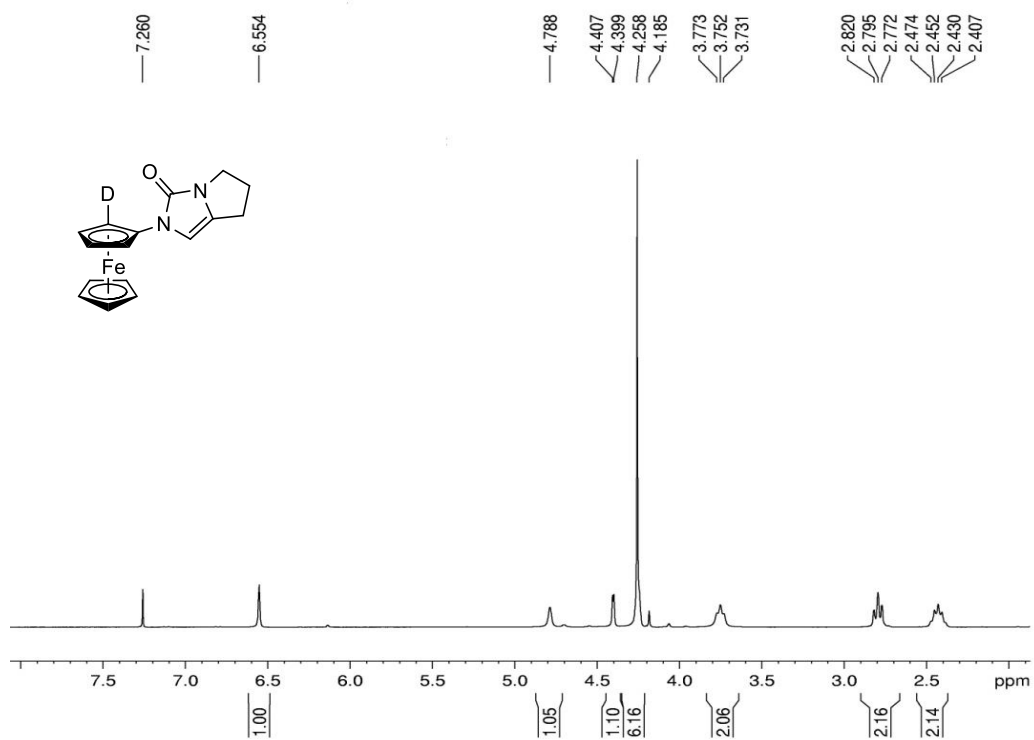
¹H spectrum for *ent*-192c.



¹H and ¹³C spectra for 2Sp-D-*syn*-**188i**.

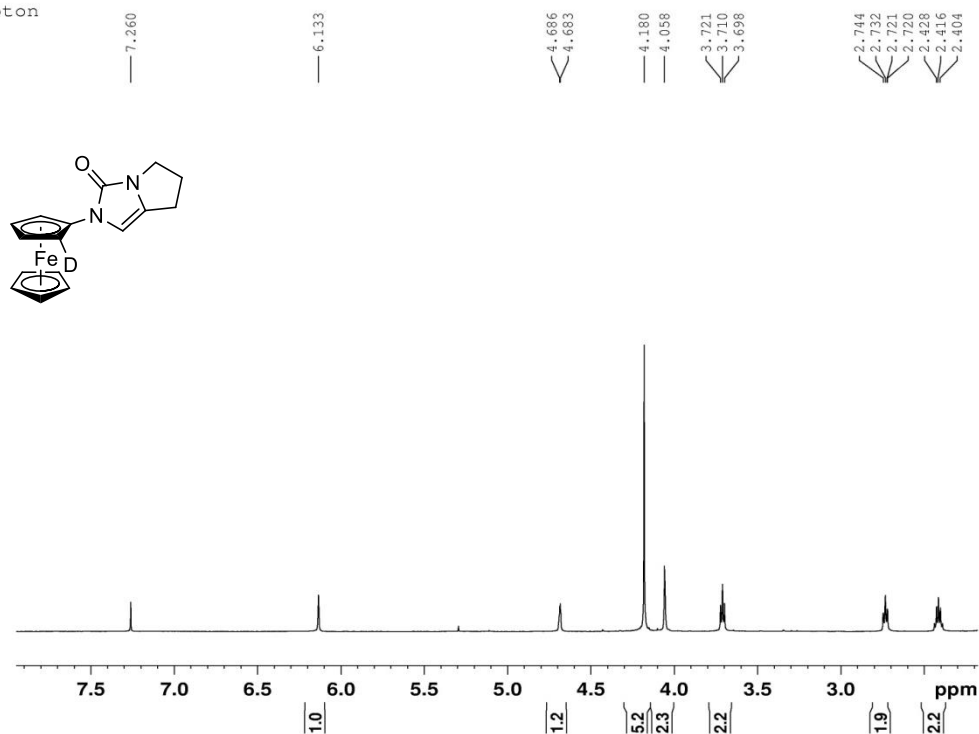


¹H and ¹³C spectra for 2*Rp*-D-**anti**-**190d**.

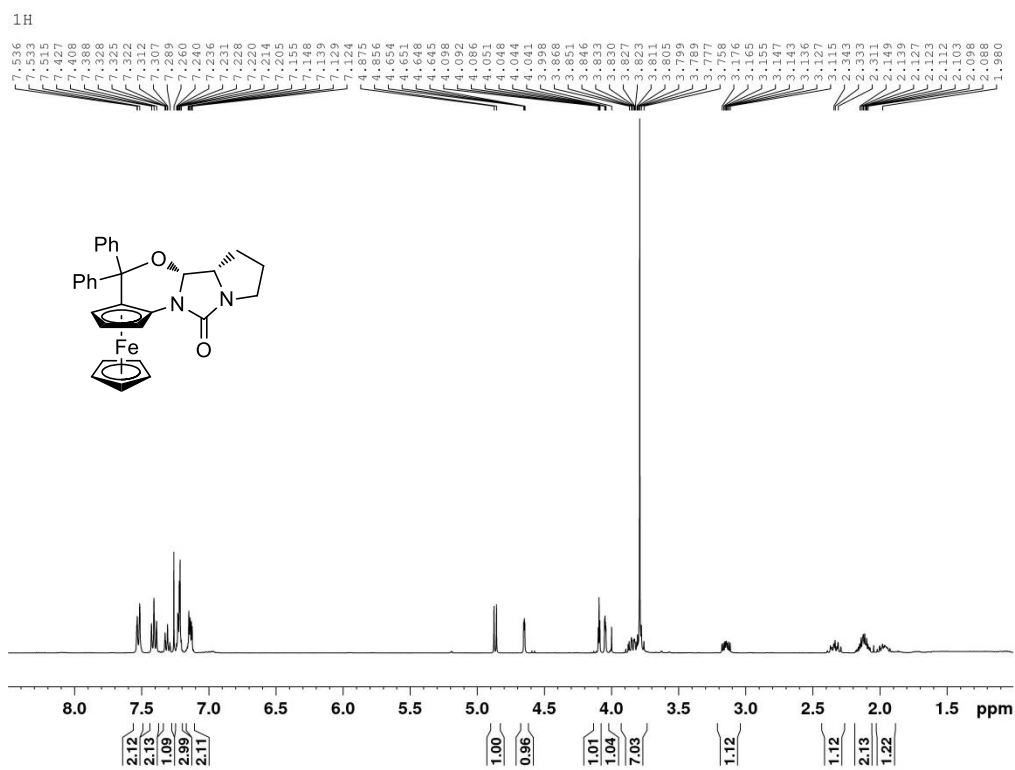


¹H and ¹³C spectra for **192d**.

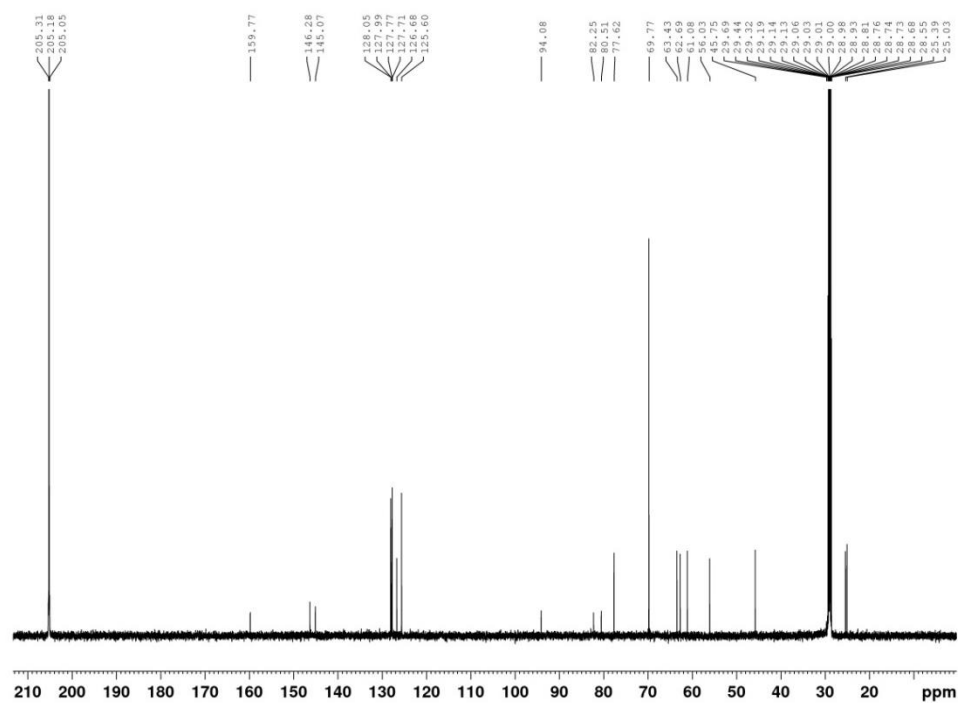
¹d proton



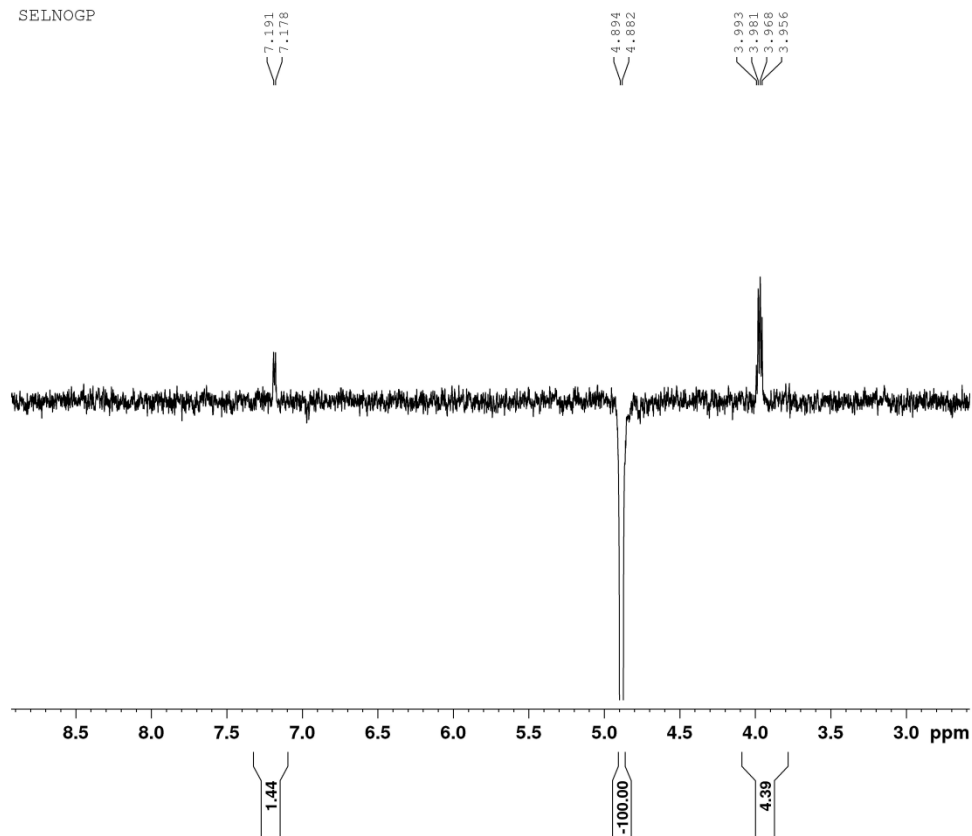
¹H spectrum for *ent*-192d.



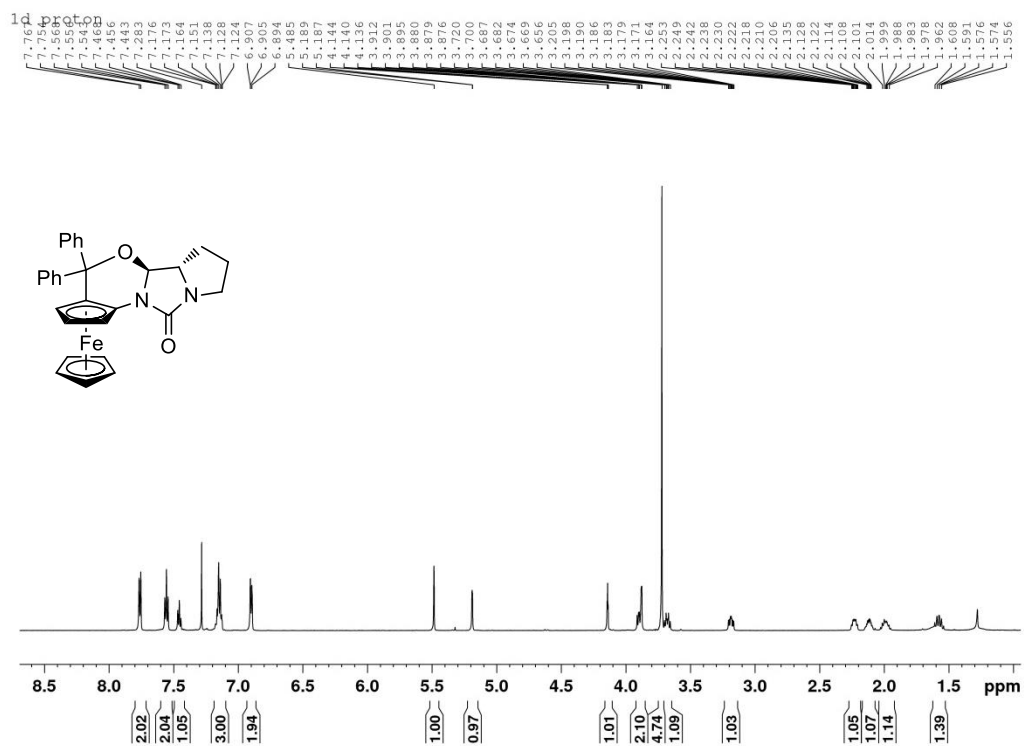
^{13}C carbon with proton decoupling



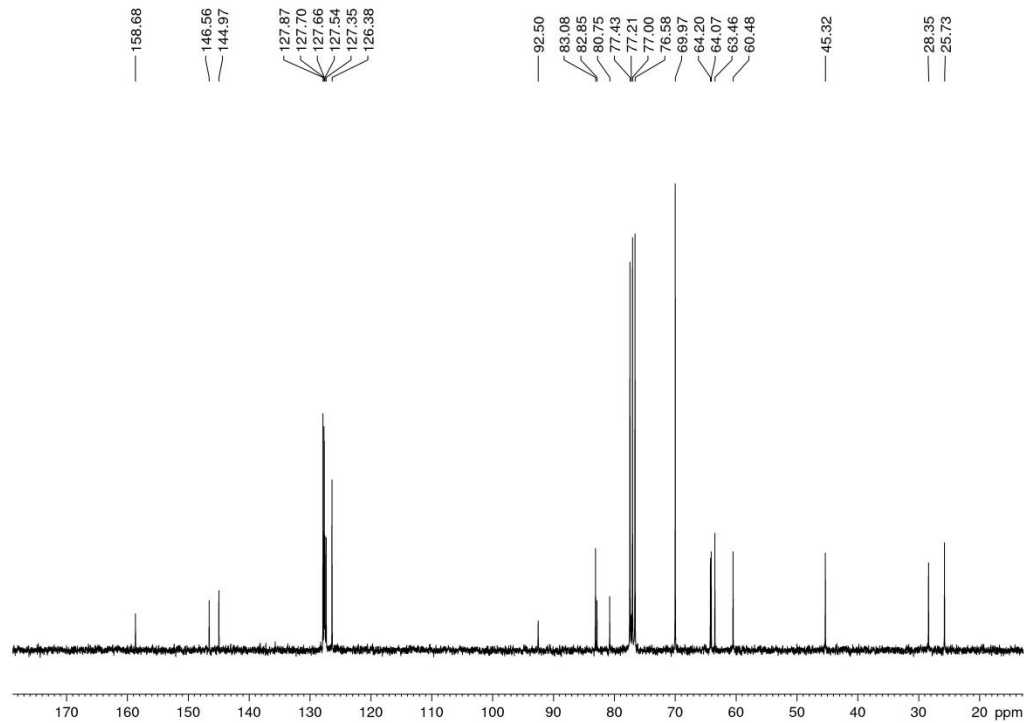
SELOGP

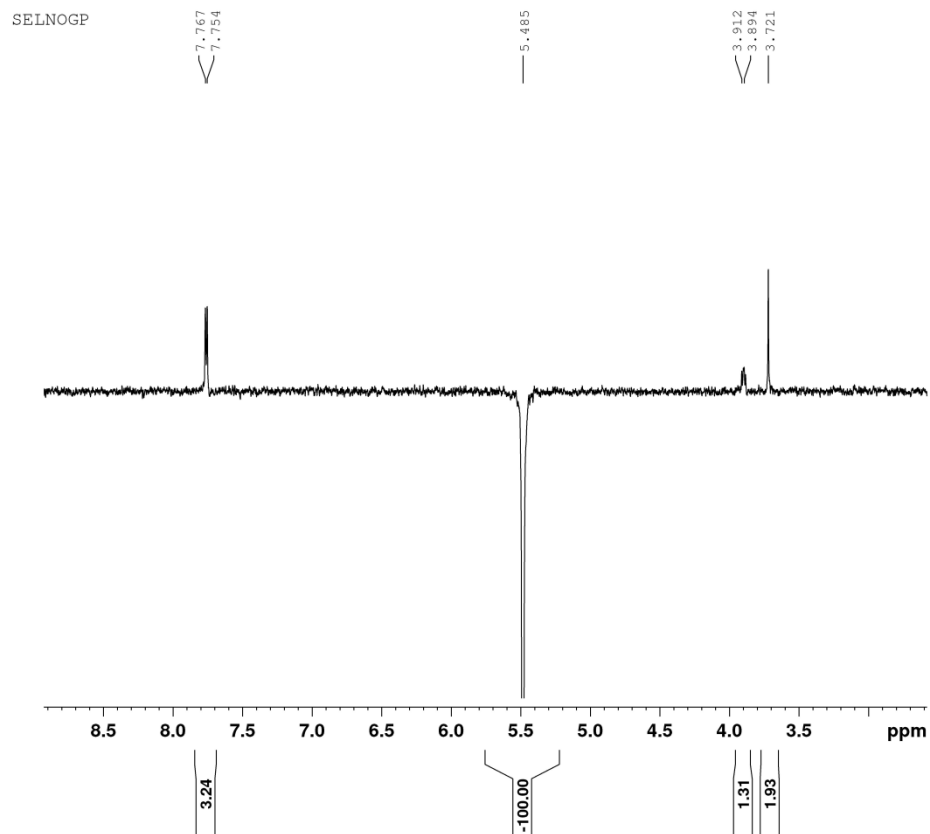


^1H , ^{13}C spectra and nOe spectra for *syn*-**194**.



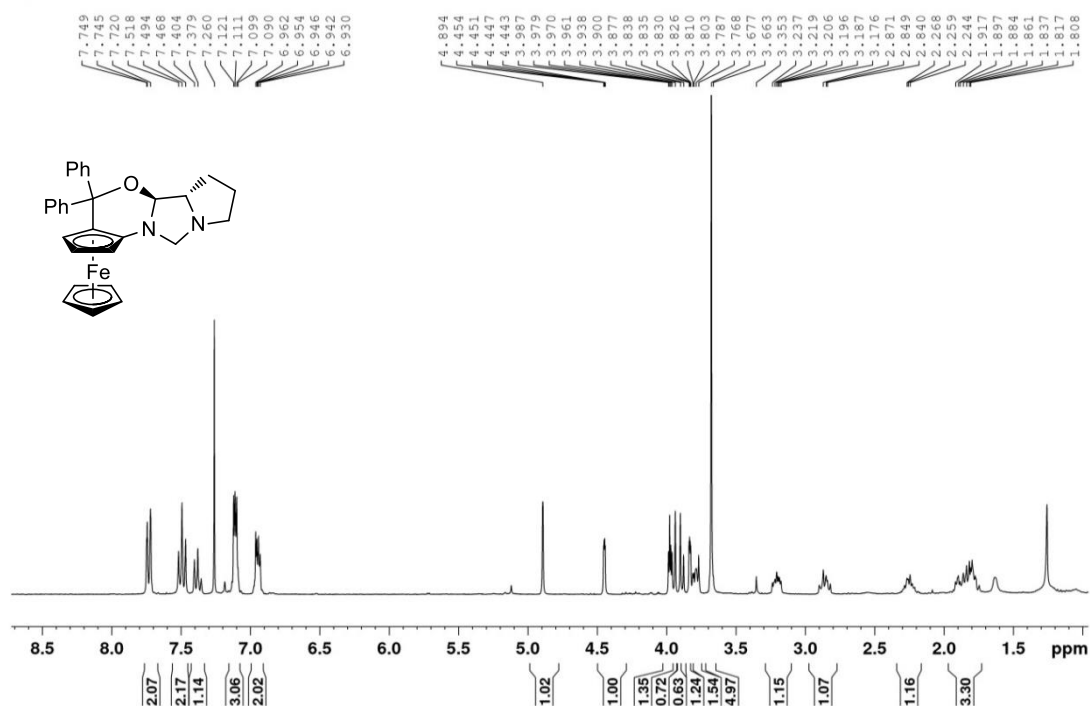
1D carbon with proton decoupling



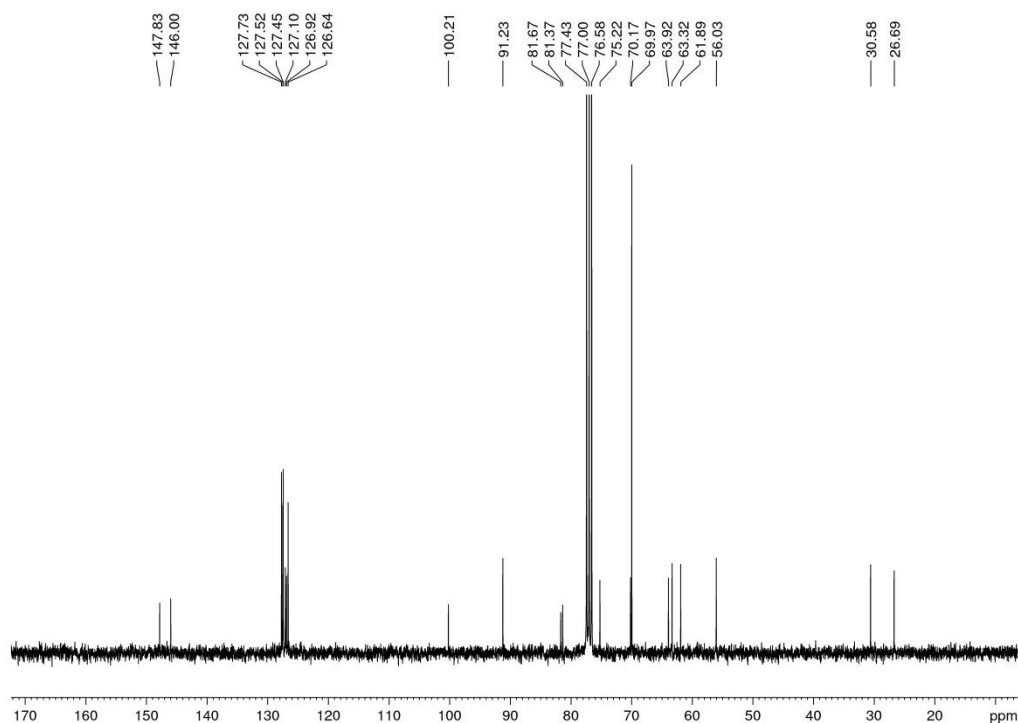


^1H , ^{13}C spectra and nOe spectra for *anti*-194.

1D proton

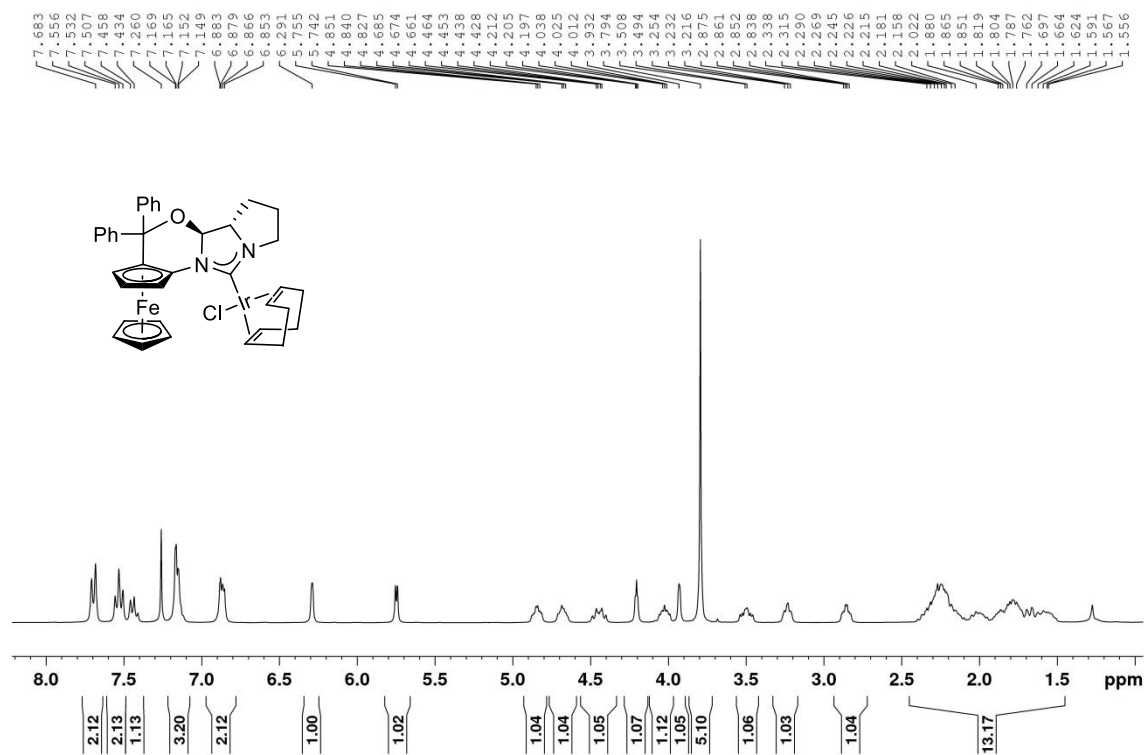


1D carbon with proton decoupling

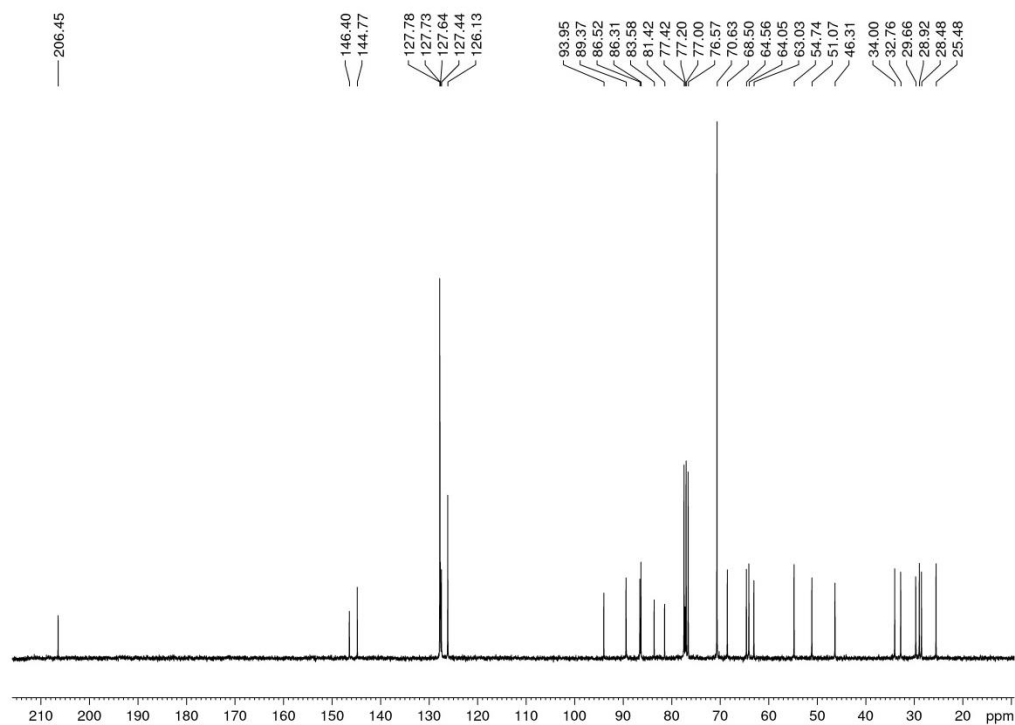


^1H and ^{13}C spectra for **195**.

1D proton

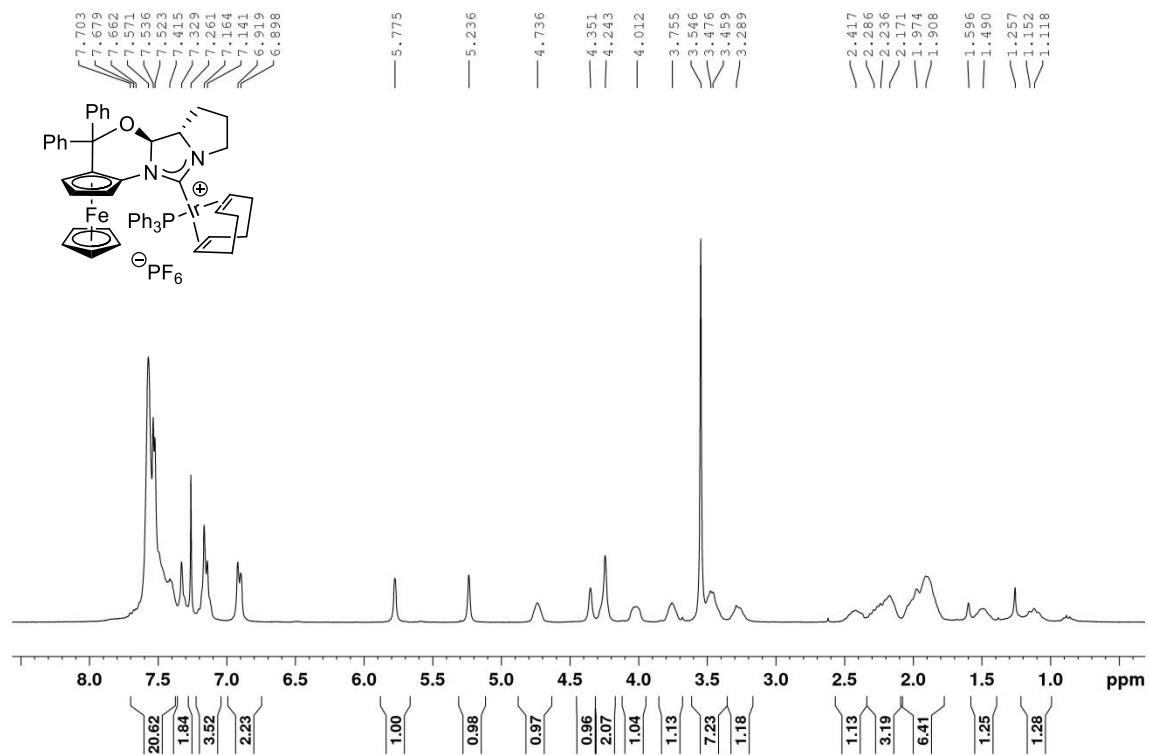


1D carbon with proton decoupling

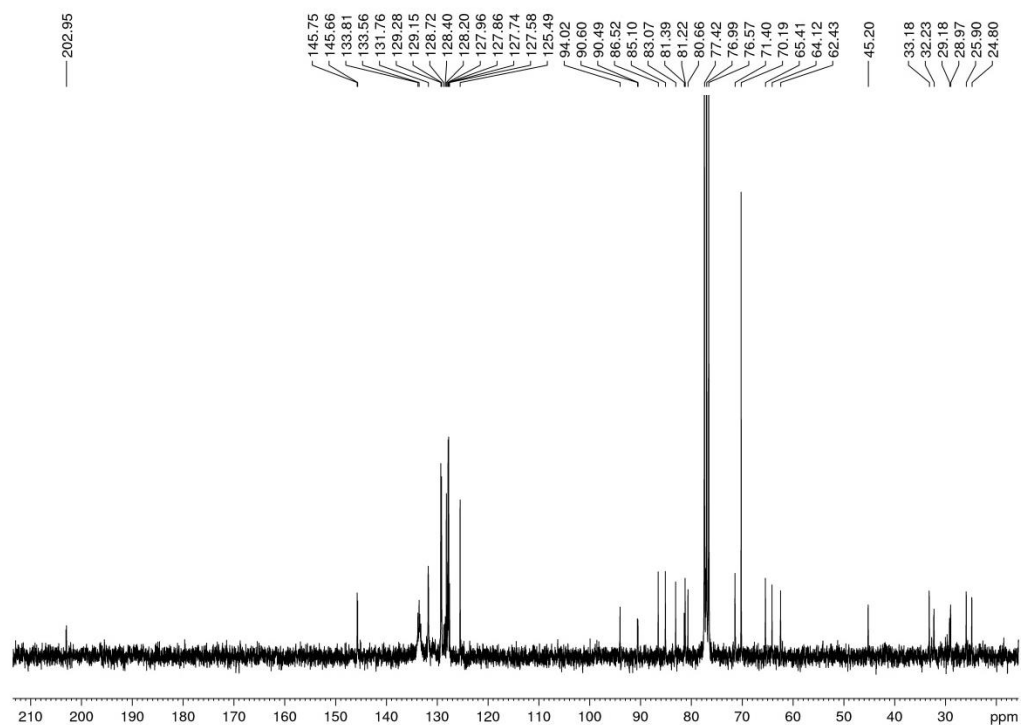


^1H and ^{13}C spectra for **197**.

1D proton

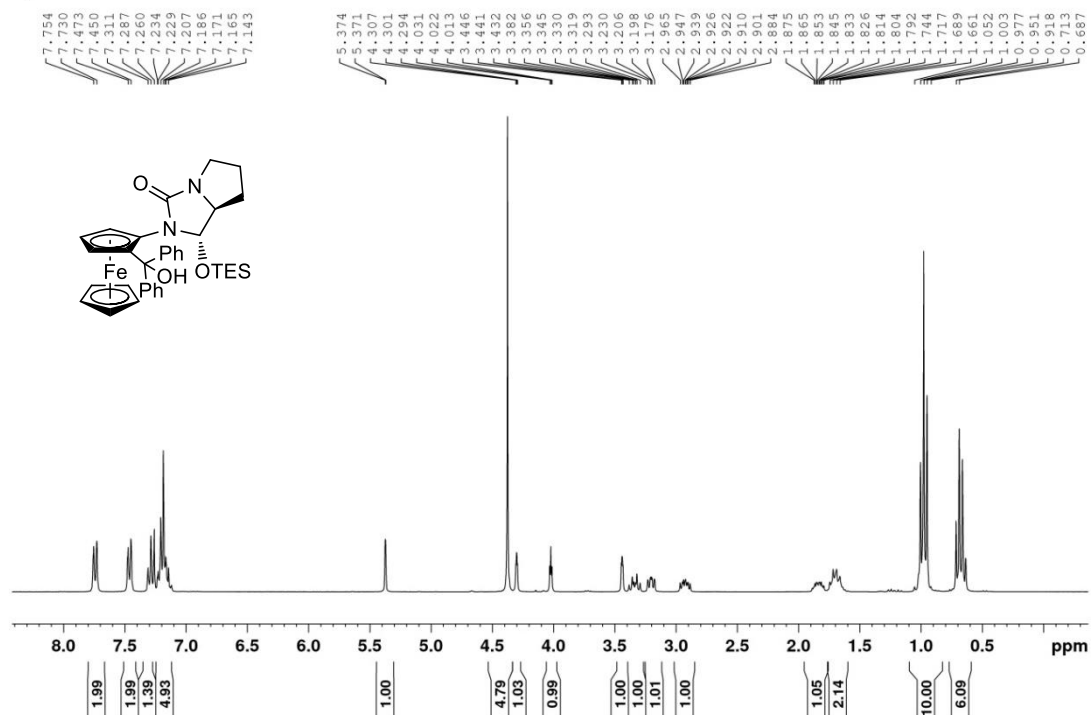


1D carbon with proton decoupling

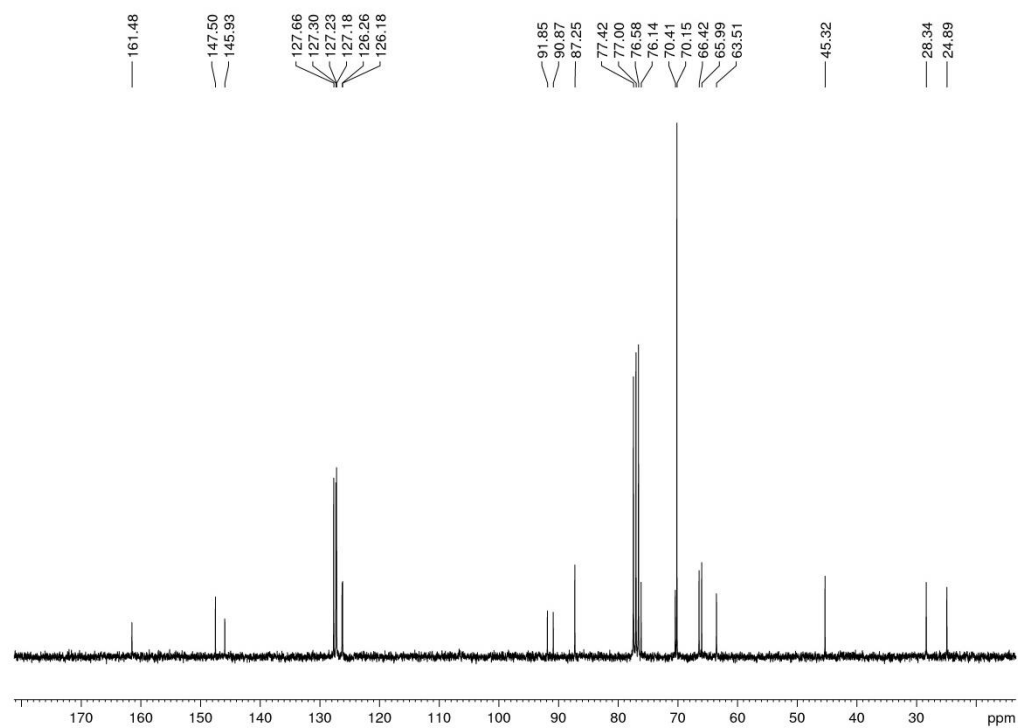


^1H and ^{13}C spectra for **198**.

1D proton

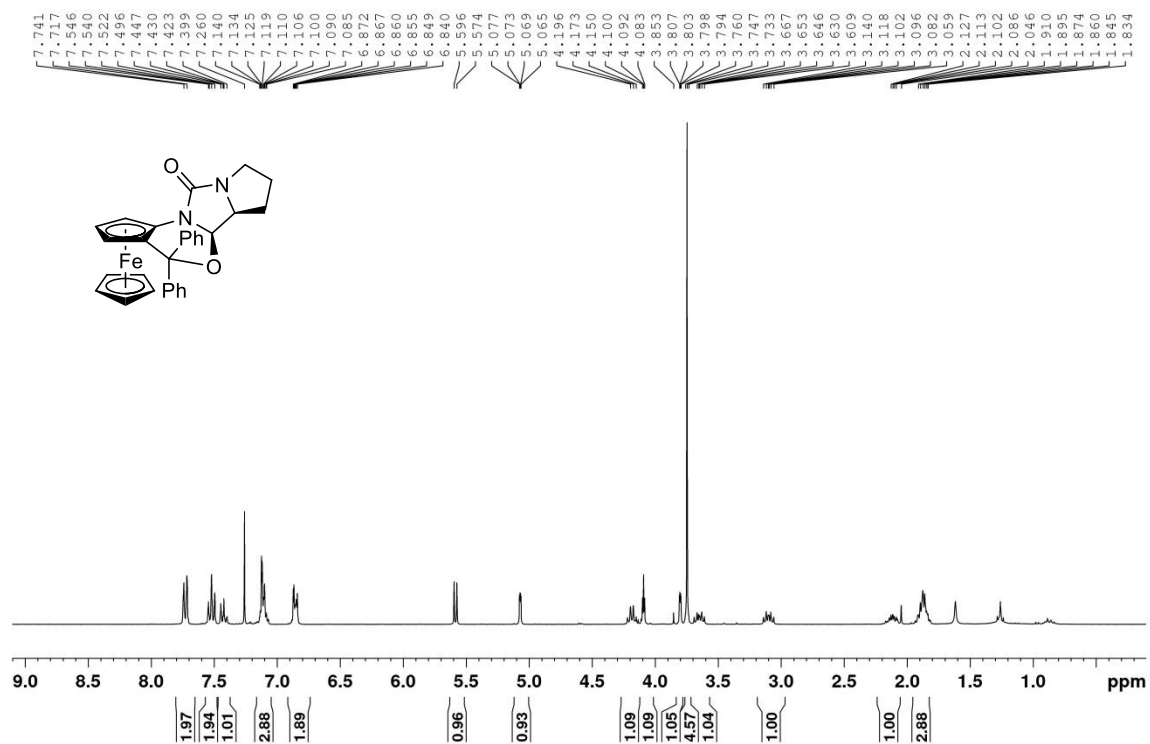


1D carbon with proton decoupling

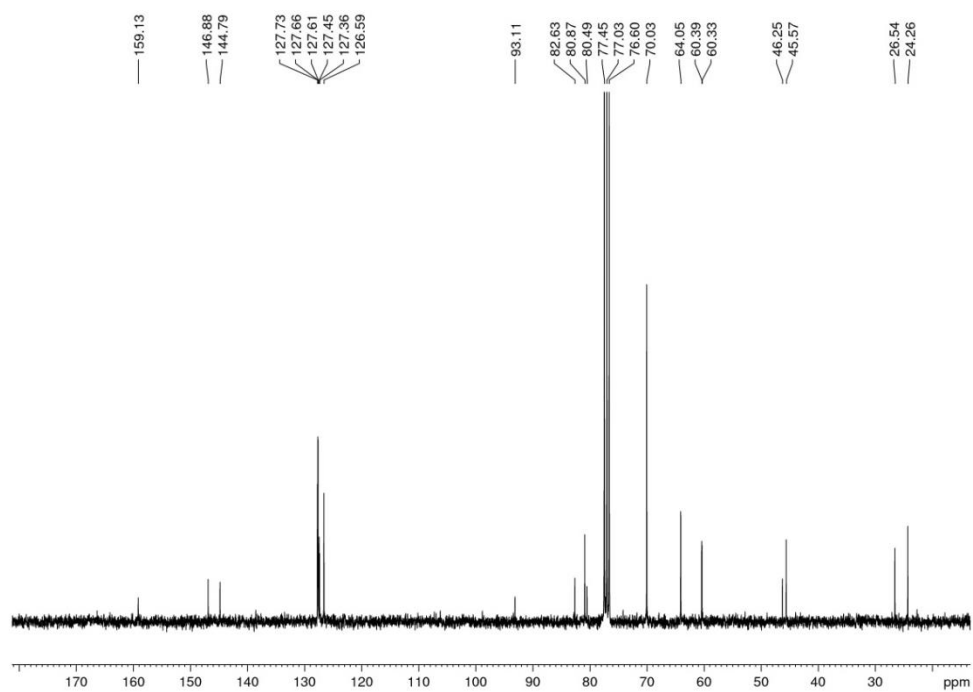


^1H and ^{13}C spectra for **190e**.

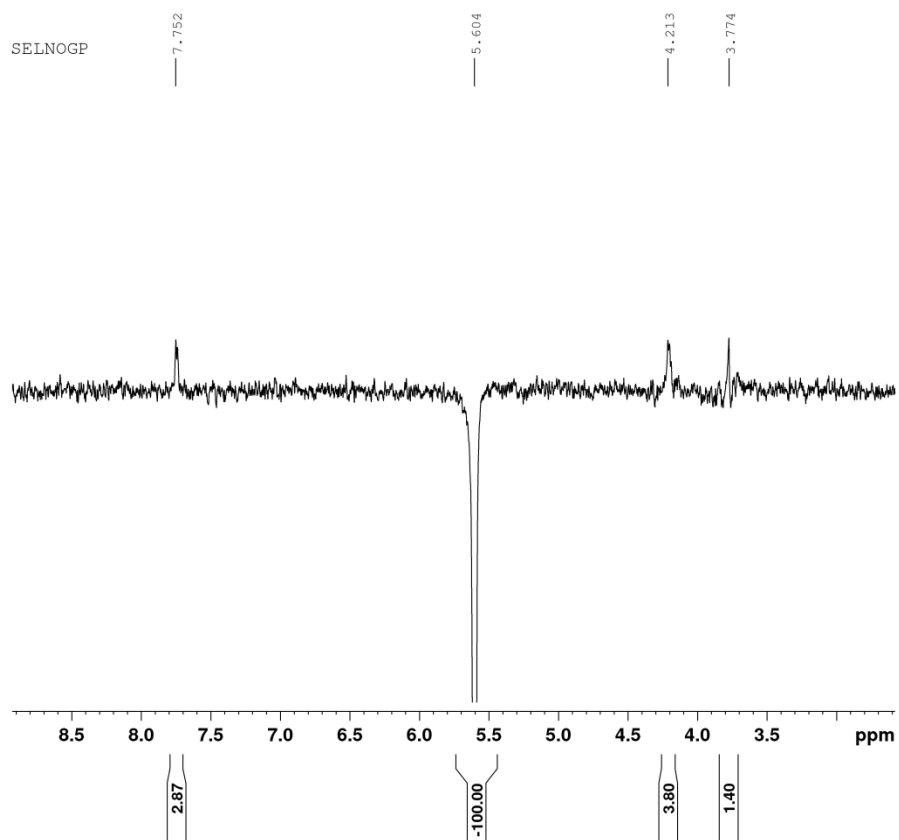
1D proton



1D carbon with proton decoupling

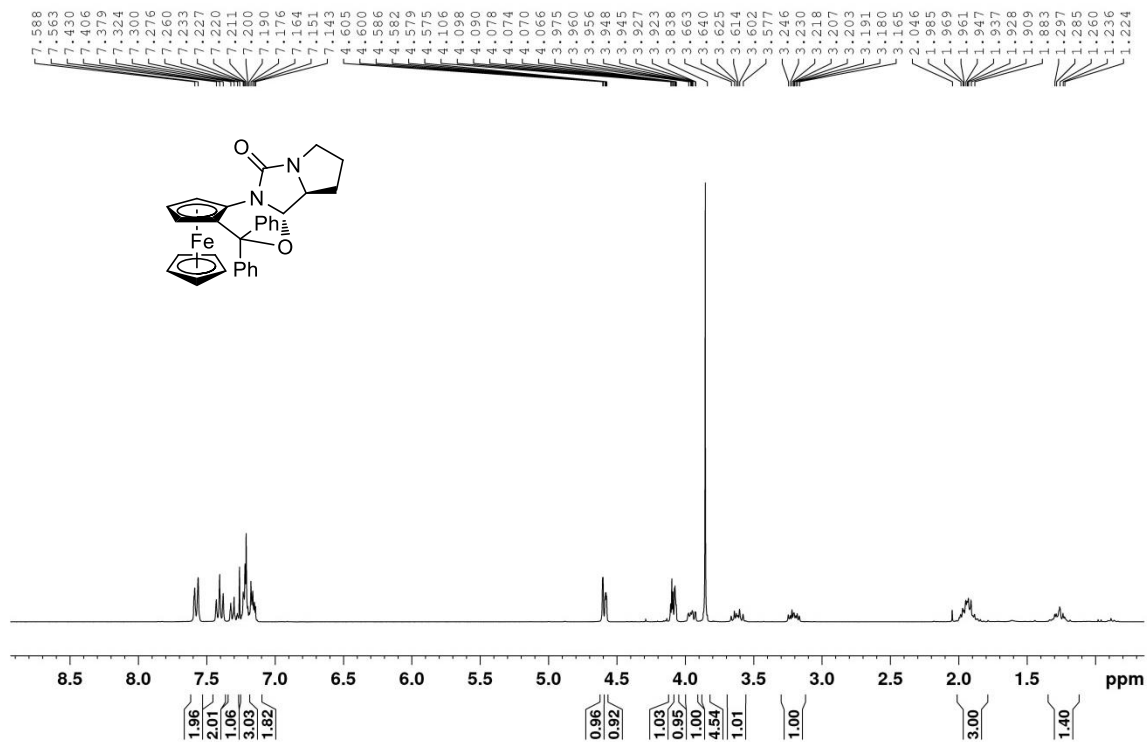


SELNOP

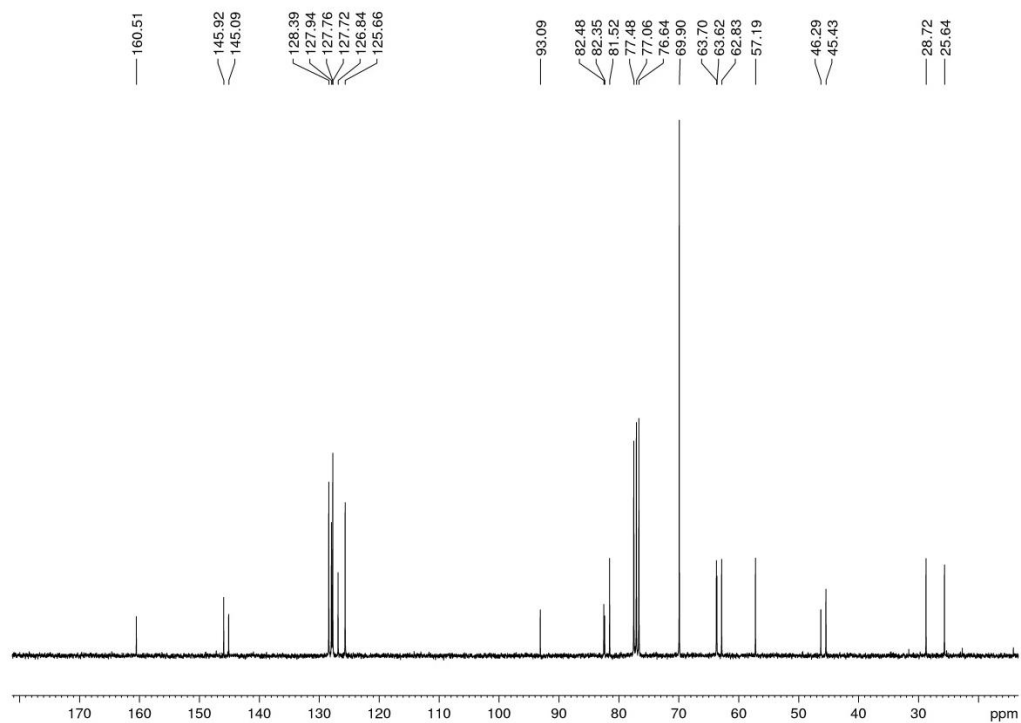


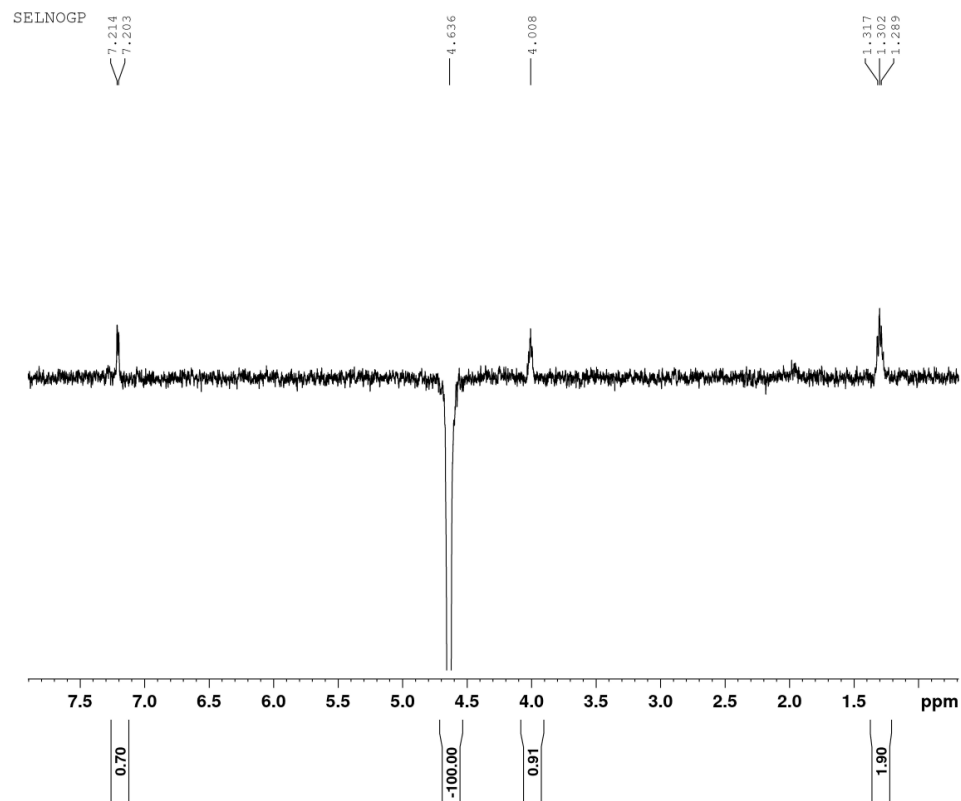
^1H , ^{13}C and nOe spectra for *syn*-**199**.

1D proton

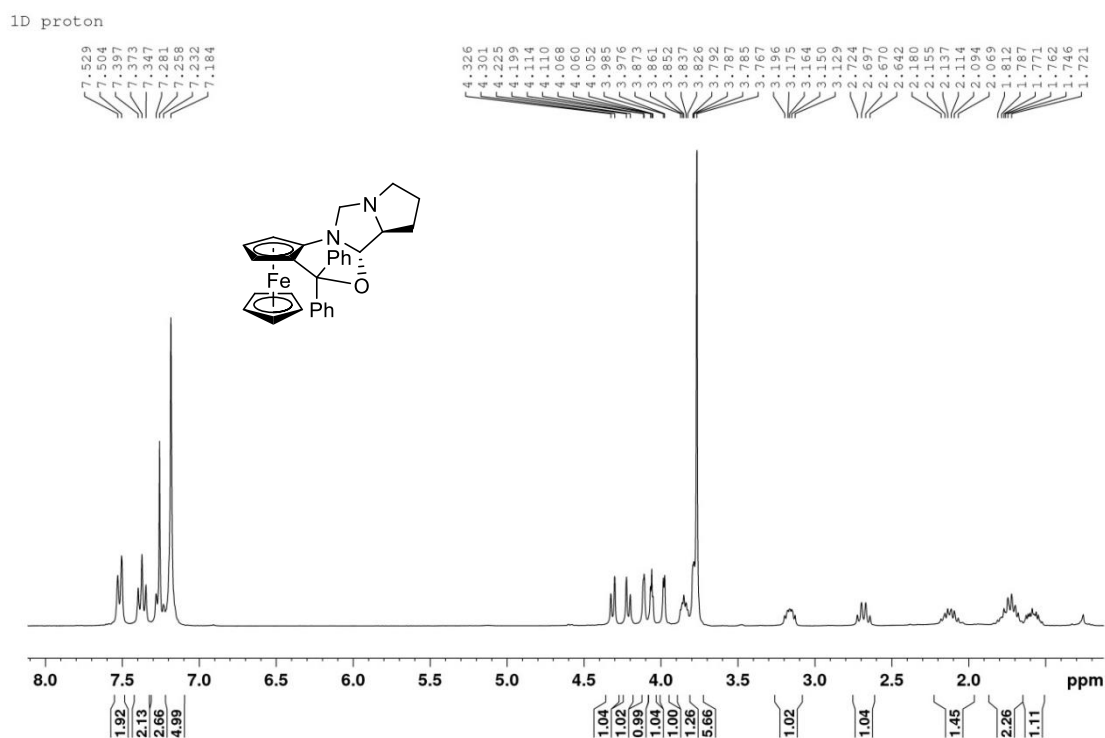


1D carbon with proton decoupling

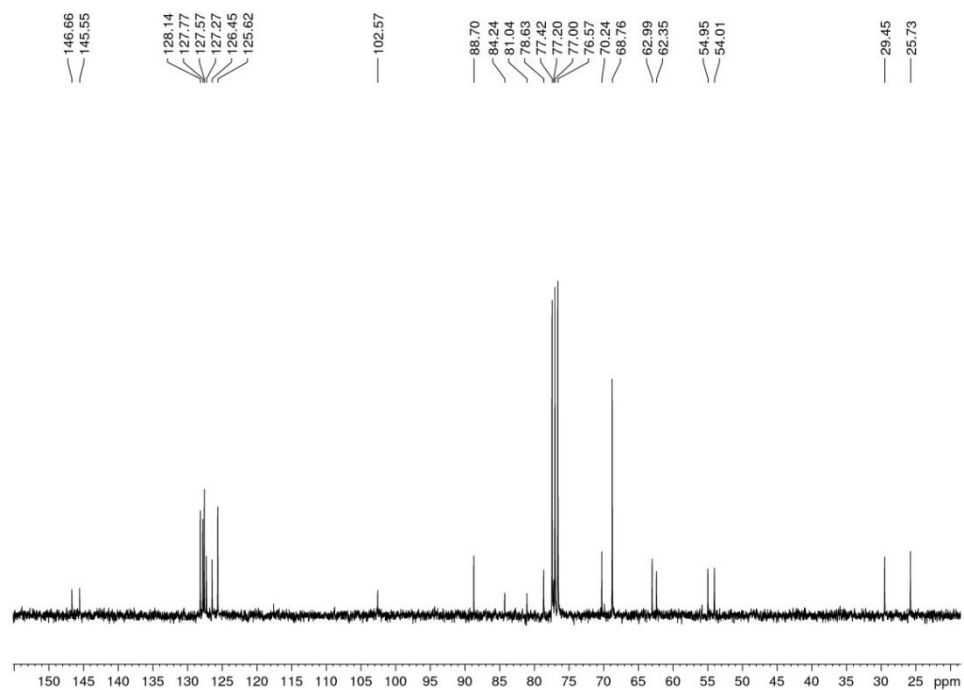




^1H , ^{13}C and nOe spectra for *anti*-**199**.

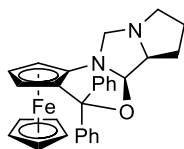
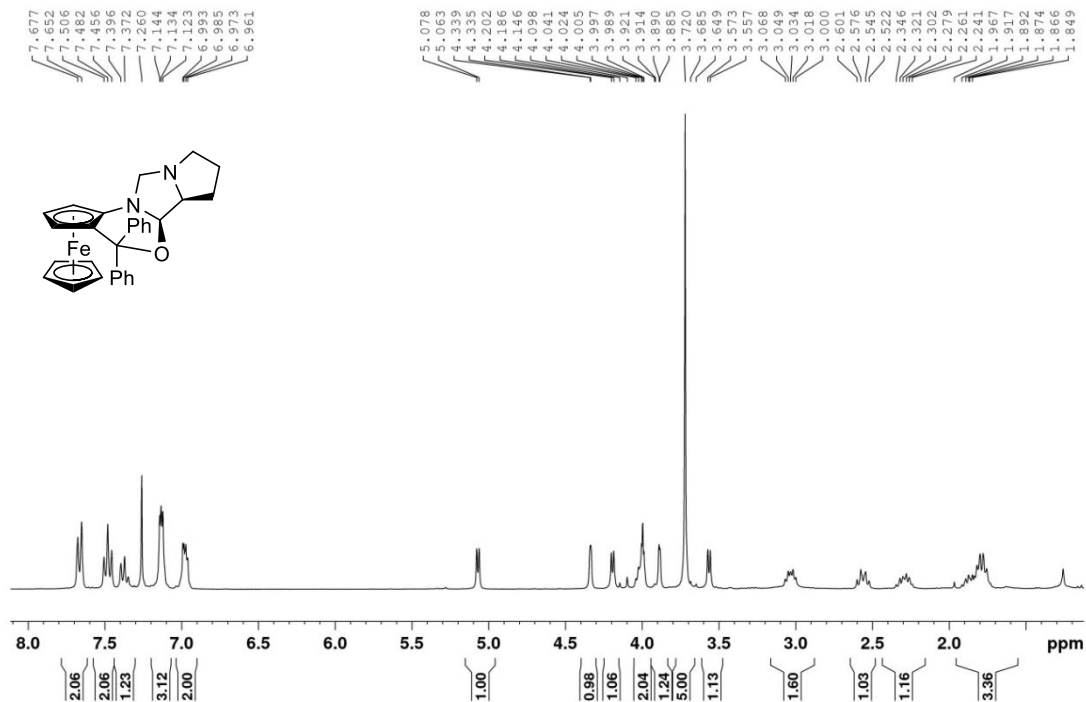


1D carbon with proton decoupling

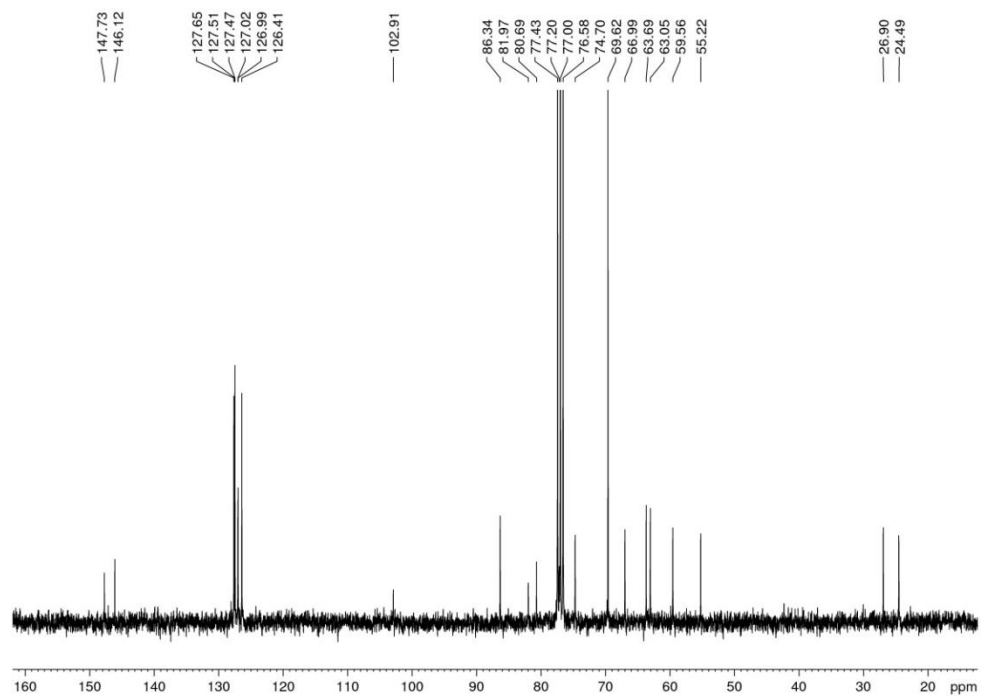


^1H and ^{13}C spectra for *anti*-200.

1D proton

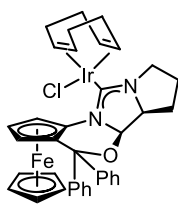
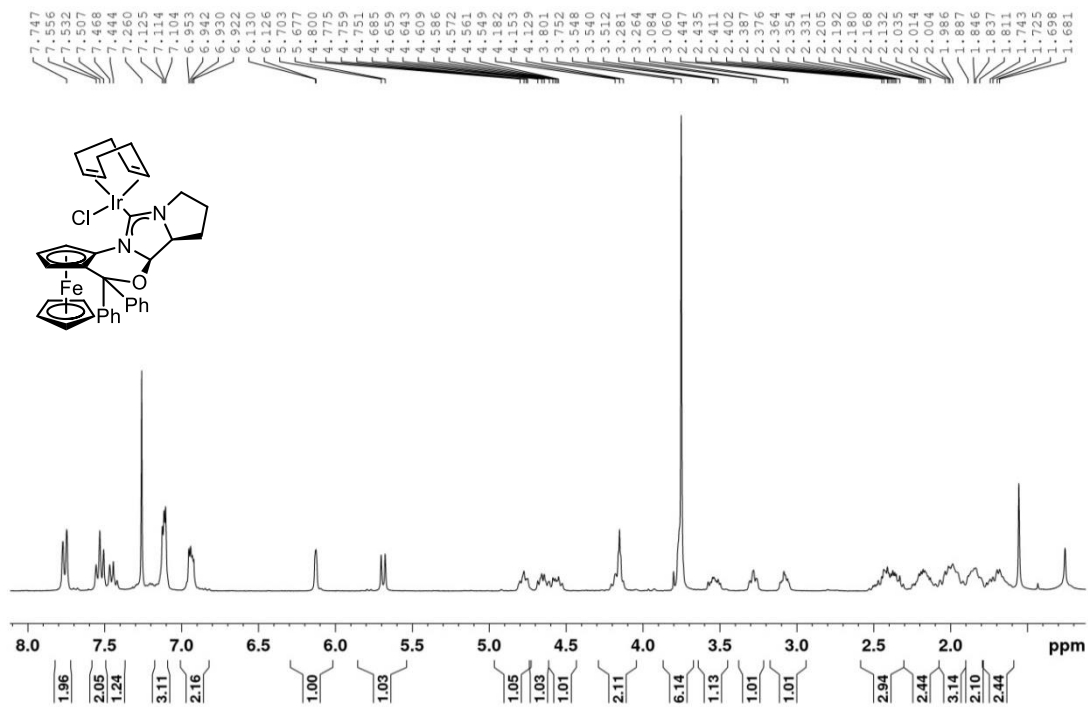


1D carbon with proton decoupling

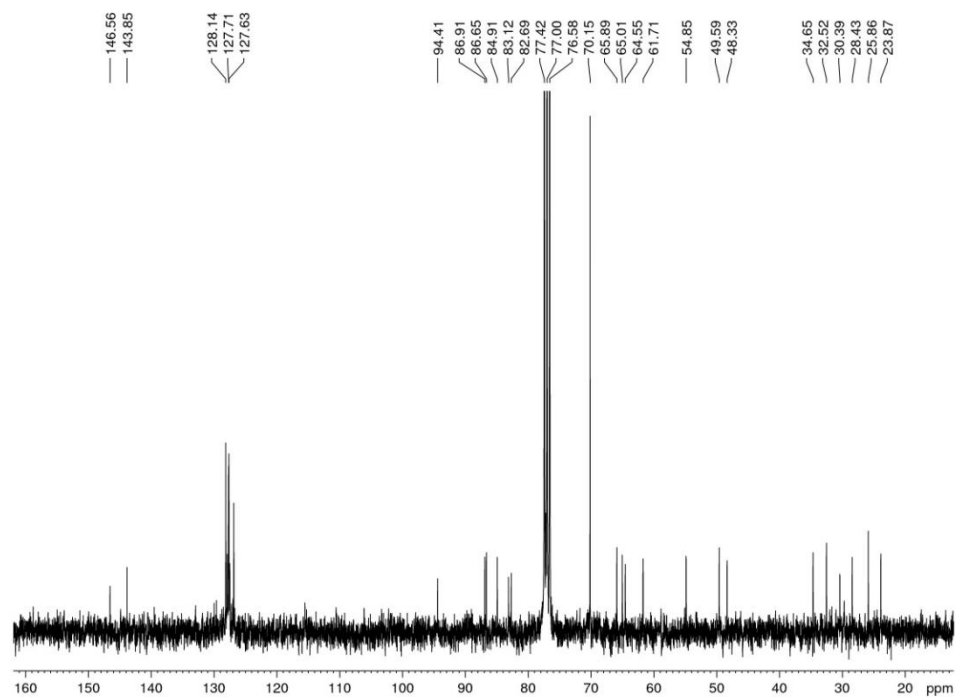


^1H and ^{13}C spectra for *syn*-200.

1D proton

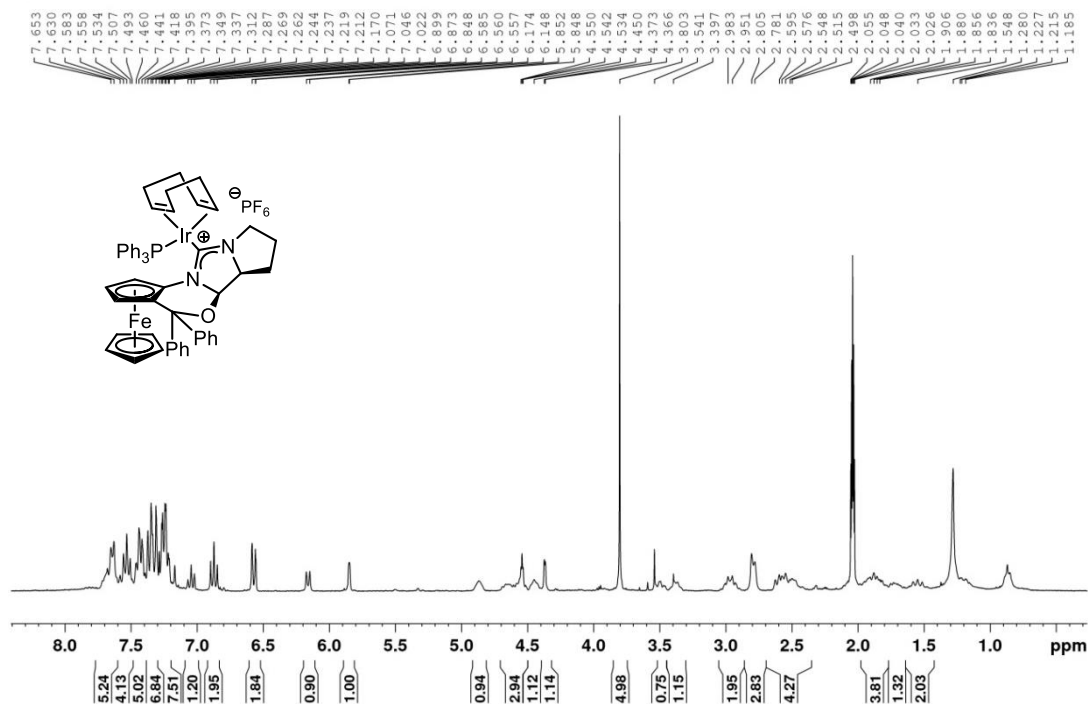


1D carbon with proton decoupling



^1H and ^{13}C spectra for **201**.

1D proton



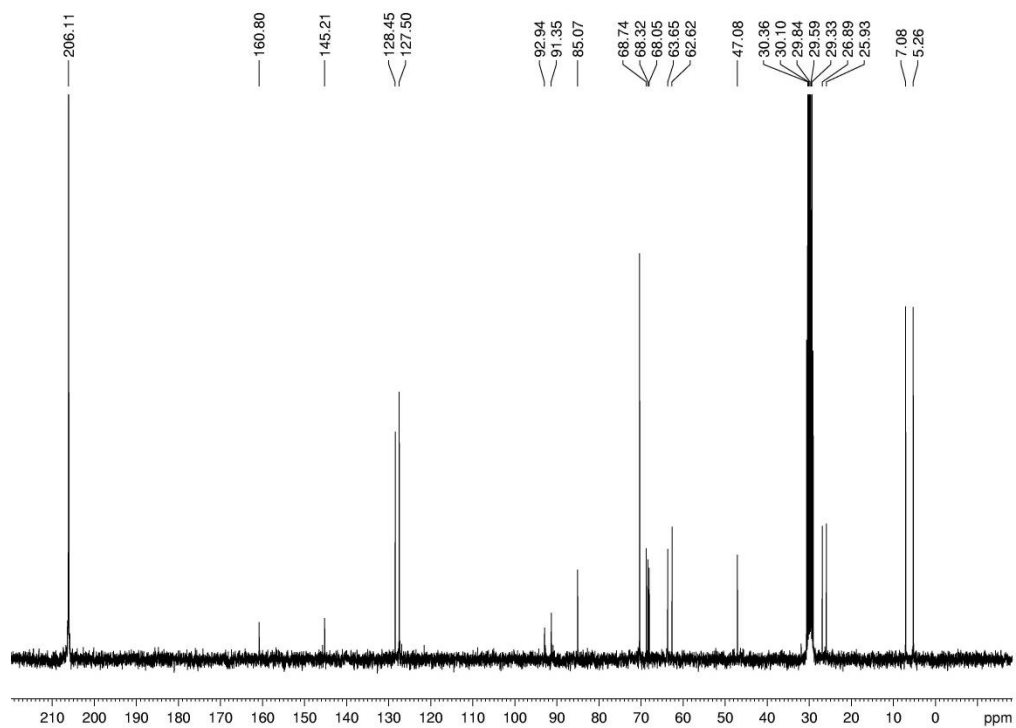
1D proton

Chemical structure of compound 1: A ferrocene derivative with a phenyl group, a hydroxyl group, and an OTES group attached to the cyclopentadienyl ring.

1D ^1H NMR spectrum (ppm) showing chemical shifts and integration values:

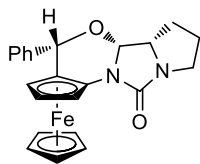
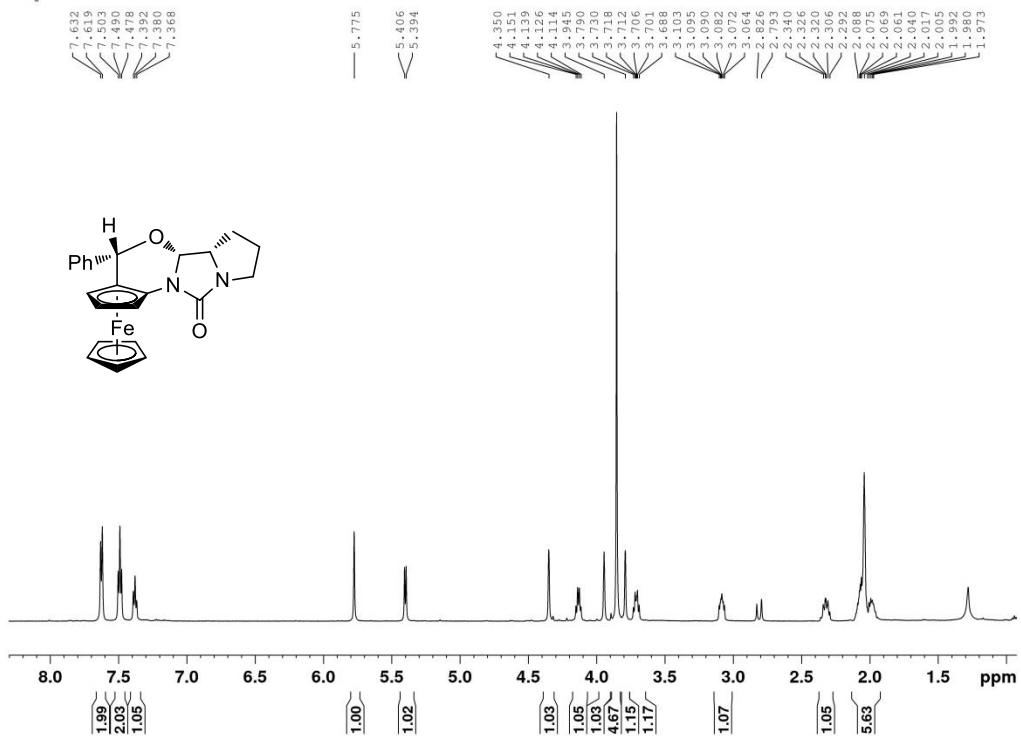
Chemical Shift (ppm)	Integration
7.369, 7.363, 7.345, 7.340, 7.290, 7.284, 7.289, 7.280, 7.269, 7.260, 7.252, 7.236	2.00, 2.03, 1.02
5.886, 5.881, 5.841, 5.815, 5.768, 5.766, 5.770, 4.565, 4.562, 4.557, 4.557, 4.419, 4.368, 4.339, 4.339, 4.106, 4.094, 4.071, 3.995, 3.987, 3.978, 3.621, 3.618, 3.603, 3.603, 3.604, 3.601, 3.595, 3.189, 3.165, 3.153, 3.139, 3.139, 3.129, 3.113, 2.853, 2.087, 2.013, 1.990, 1.853, 1.837, 1.837, 1.815, 0.882, 0.856, 0.830, 0.745, 0.741, 0.720, 0.514, 0.495, 0.487	0.75, 1.03, 0.97, 0.98, 4.64, 1.07, 1.00, 2.01, 1.06, 3.04, 1.20, 9.27, 6.16

1D carbon with proton decoupling

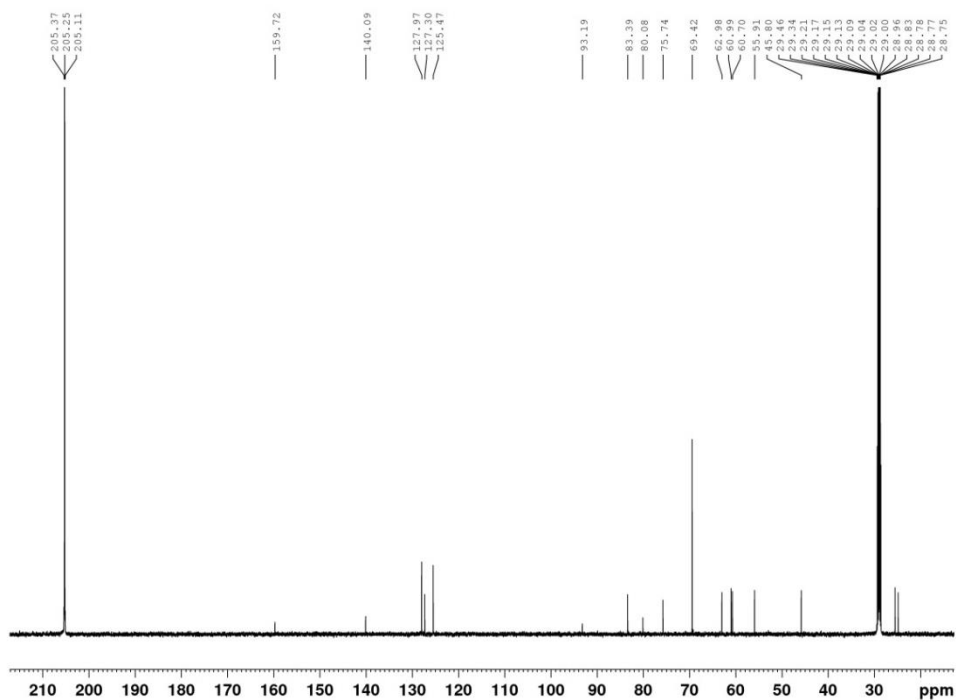


^1H and ^{13}C spectra for **188j**.

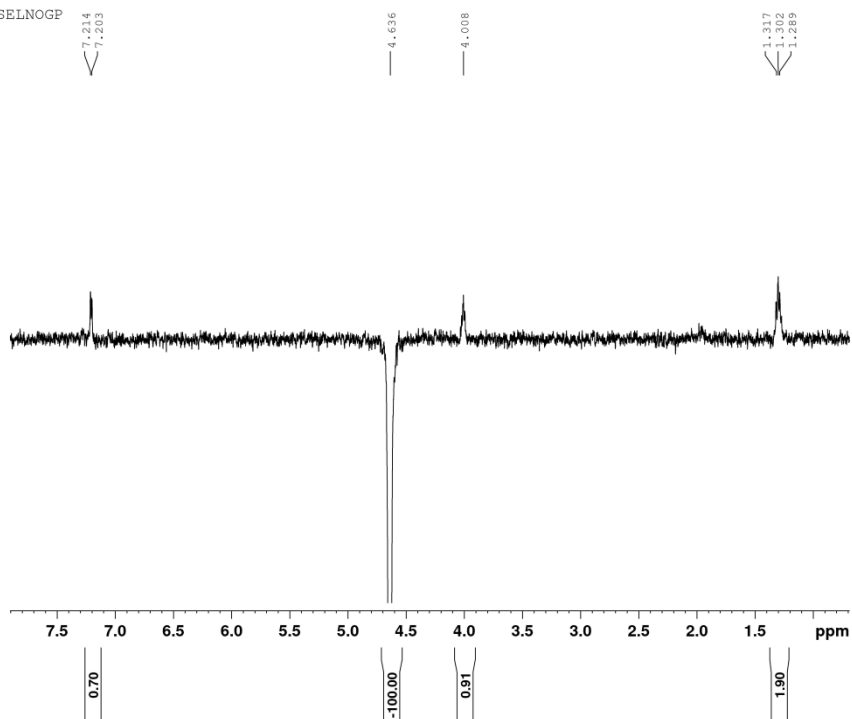
1d proton



1d carbon with proton decoupling

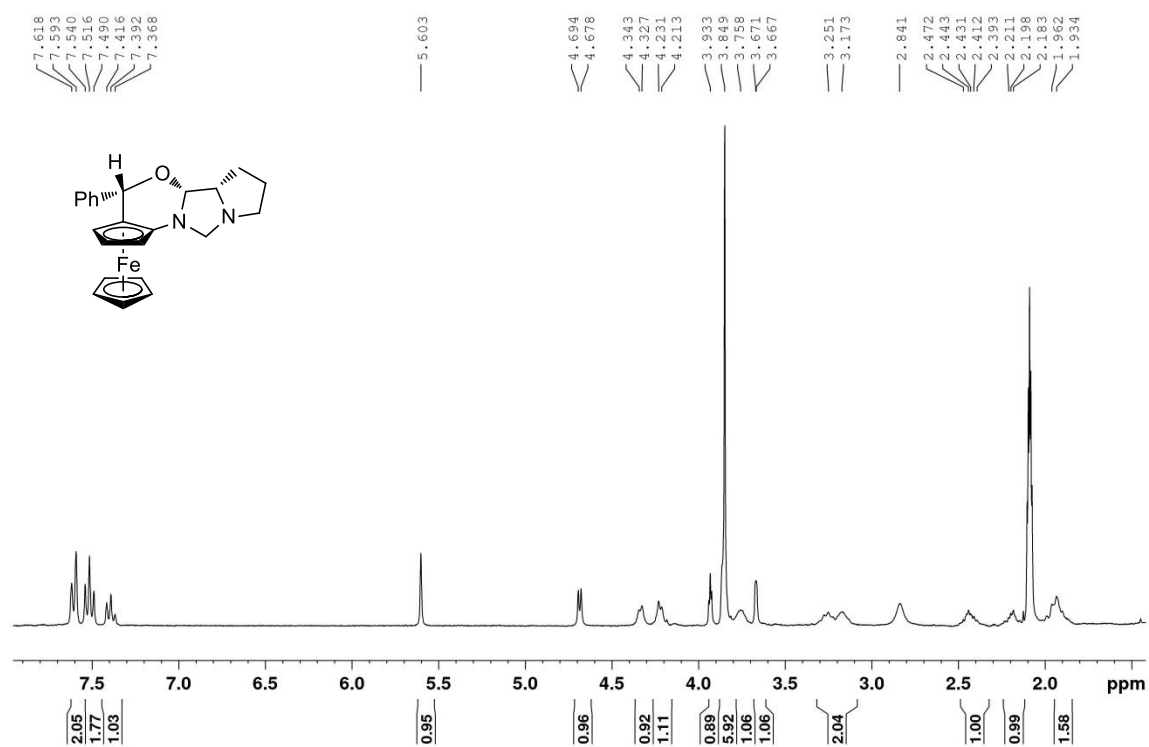


SELNOGP

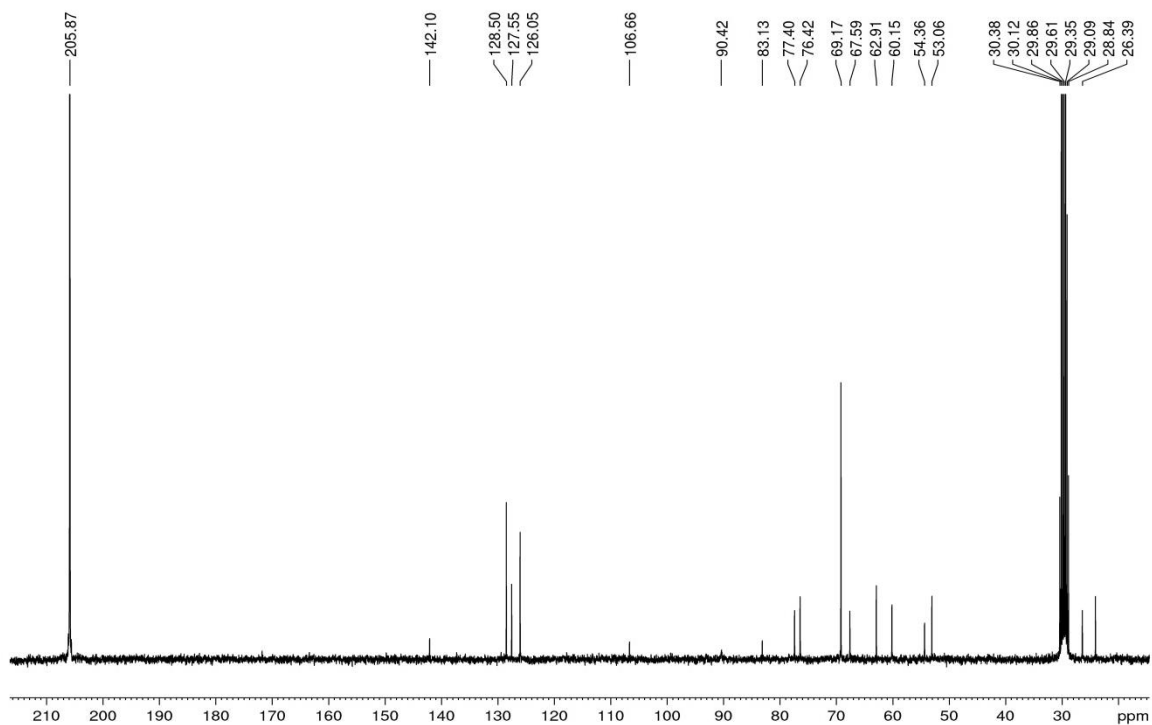


^1H , ^{13}C and nOe spectra for **204**.

1D proton

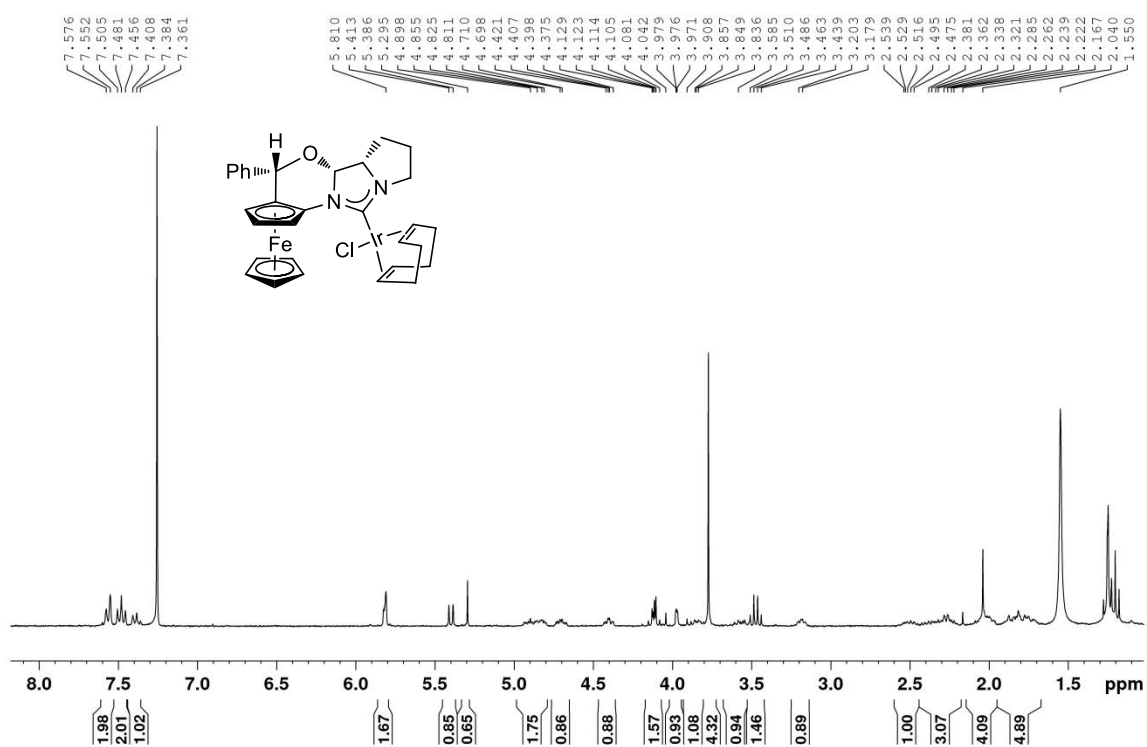


1D carbon with proton decoupling

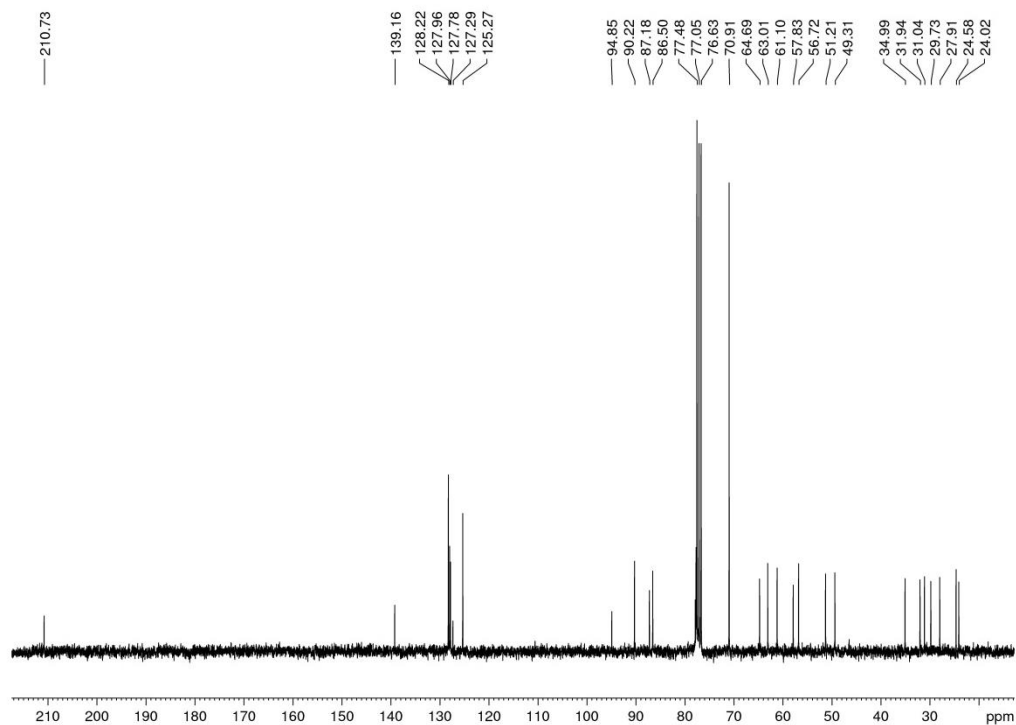


^1H and ^{13}C spectra for **205**.

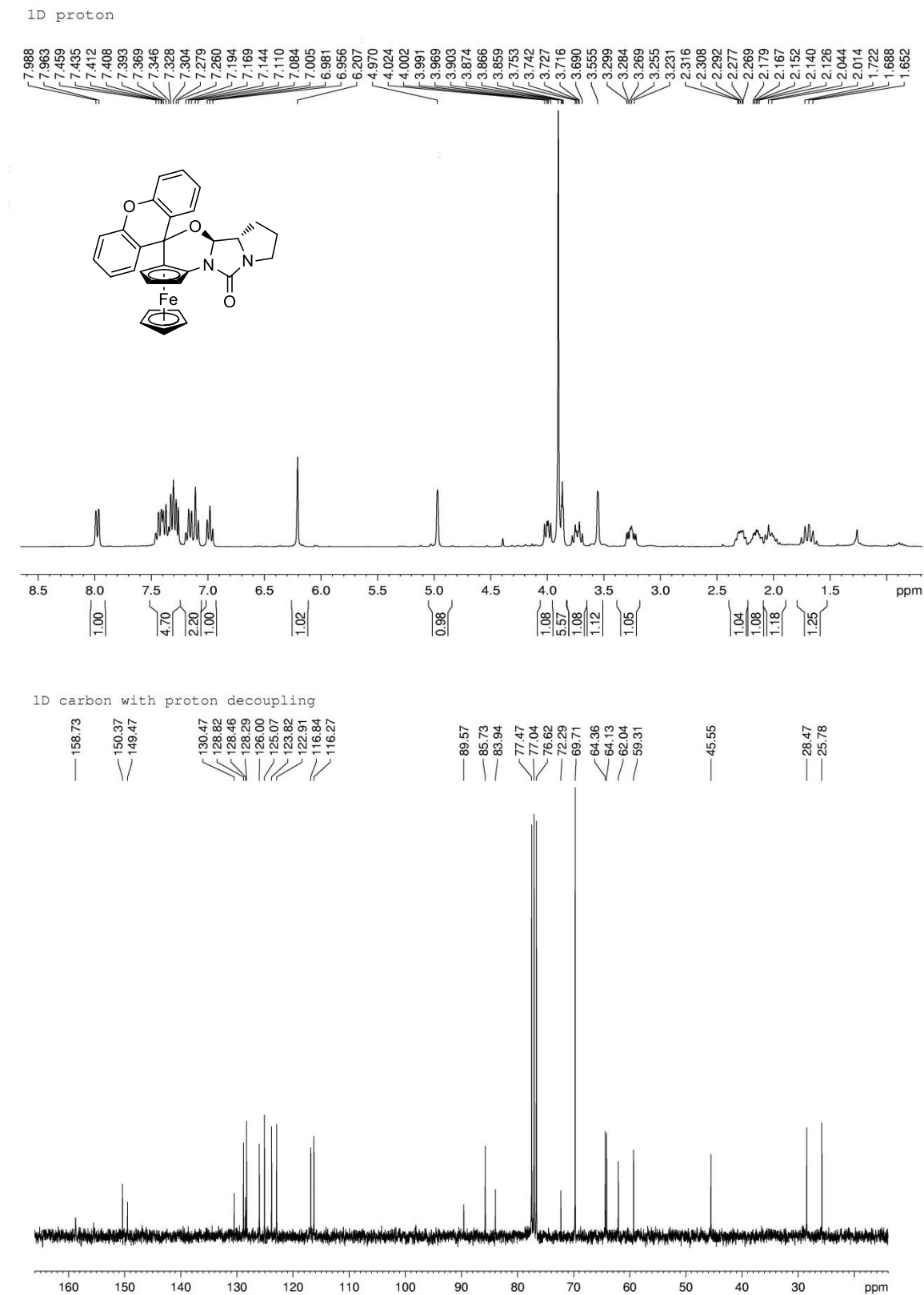
1D proton

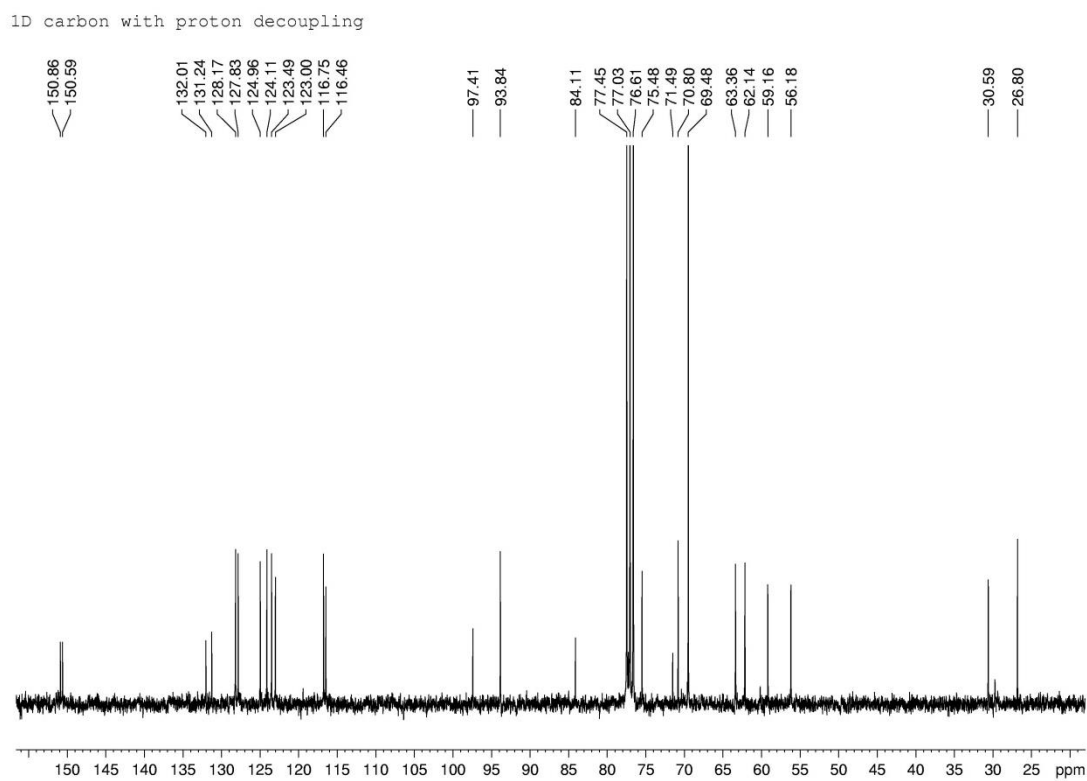
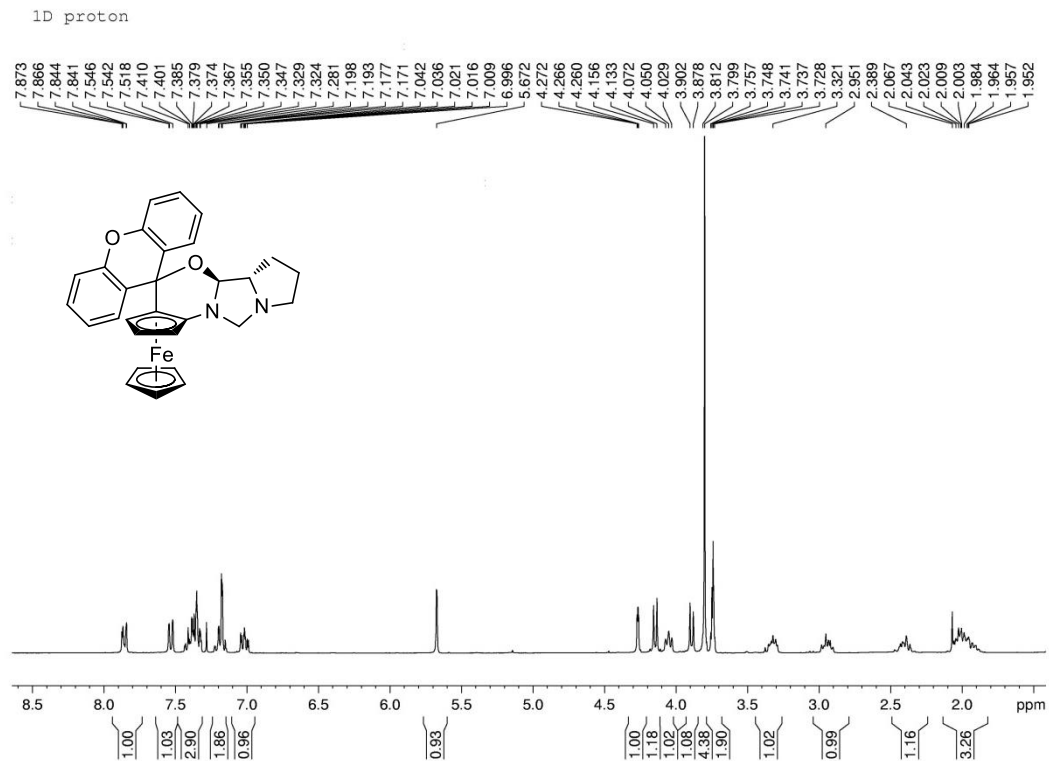


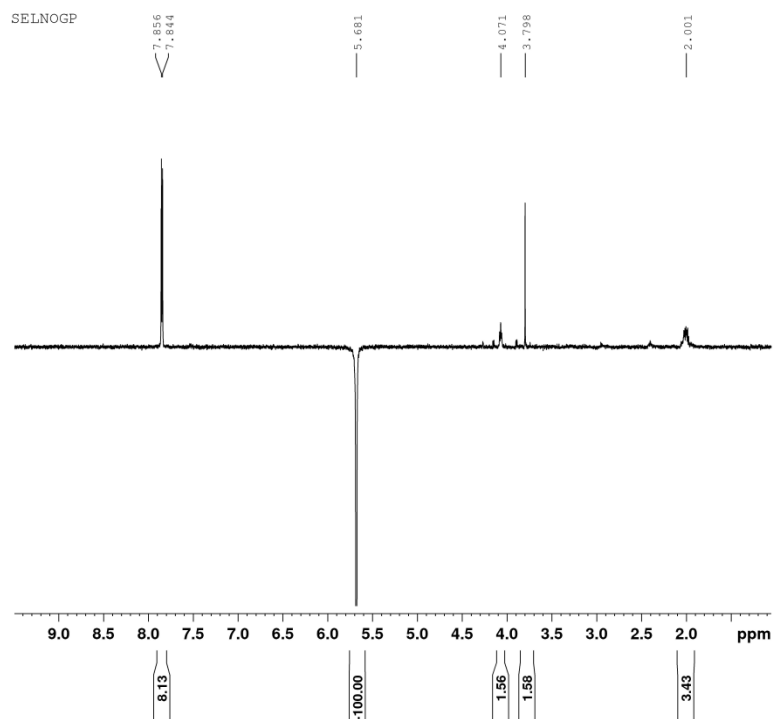
1D carbon with proton decoupling



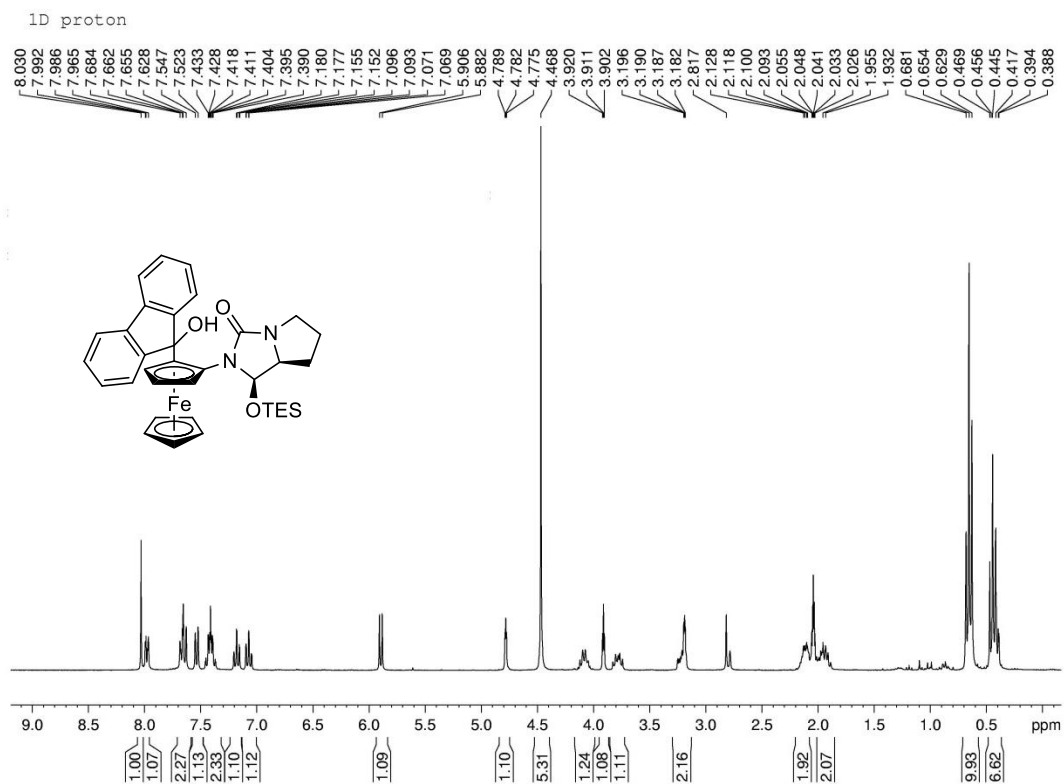
^1H and ^{13}C spectra for **207**.



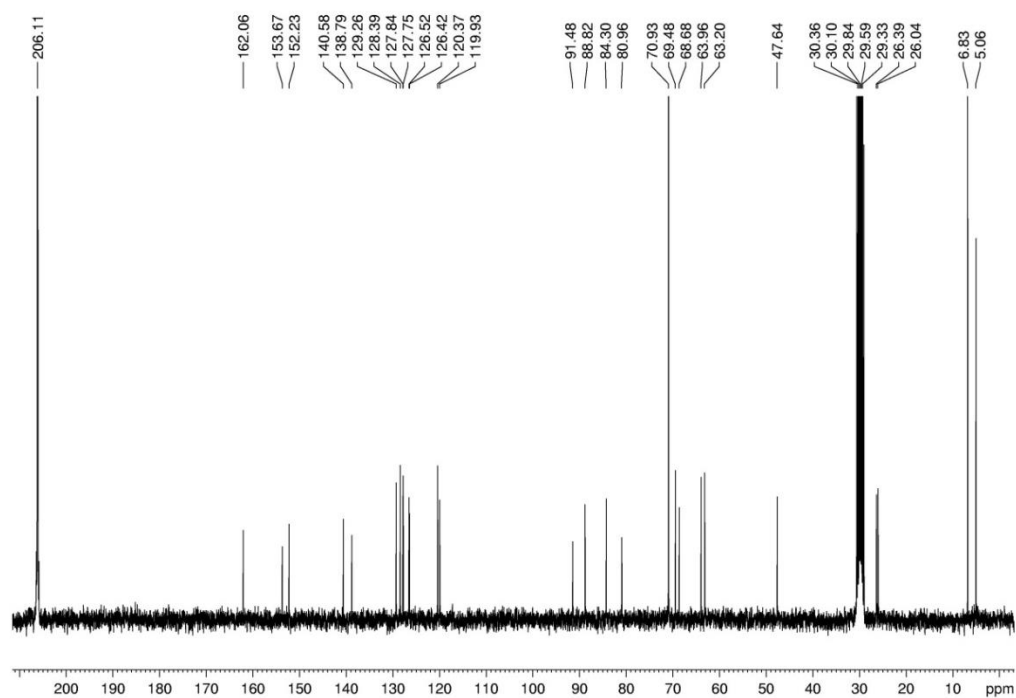




^1H , ^{13}C and nOe spectra for **210**.

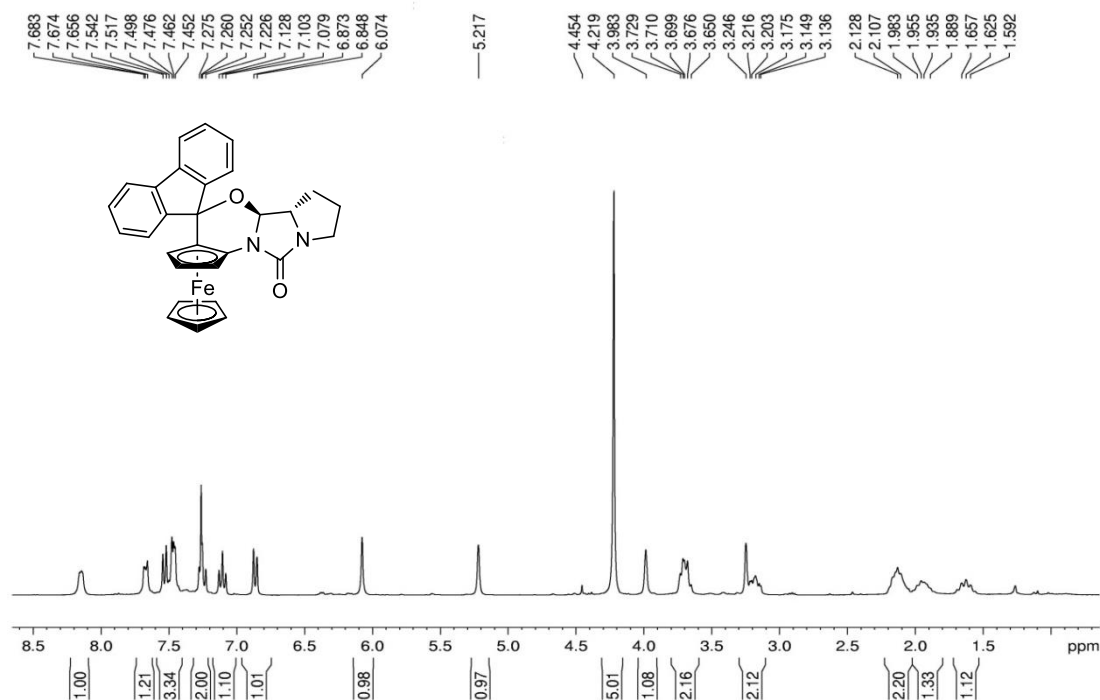


1D carbon with proton decoupling

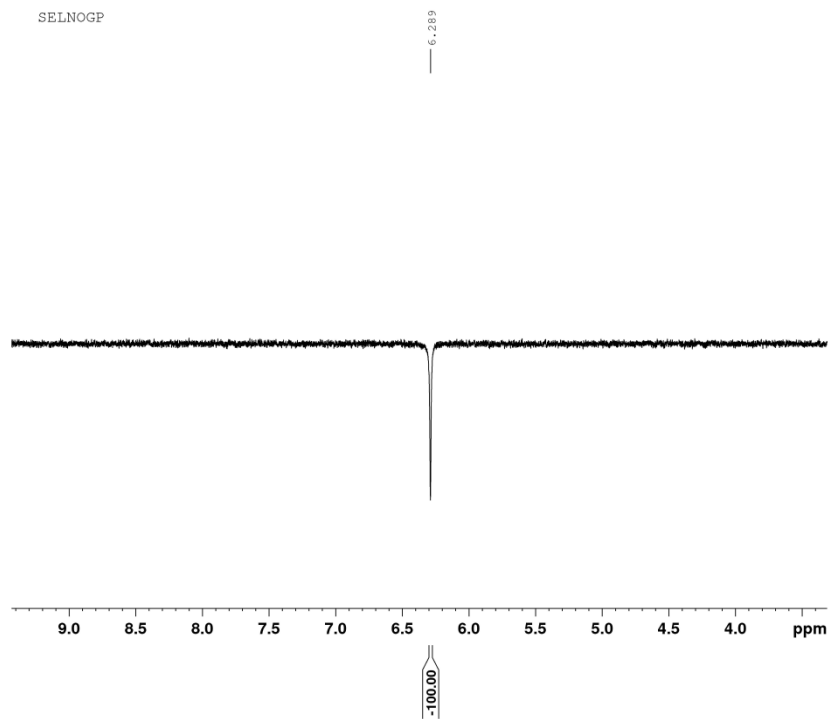
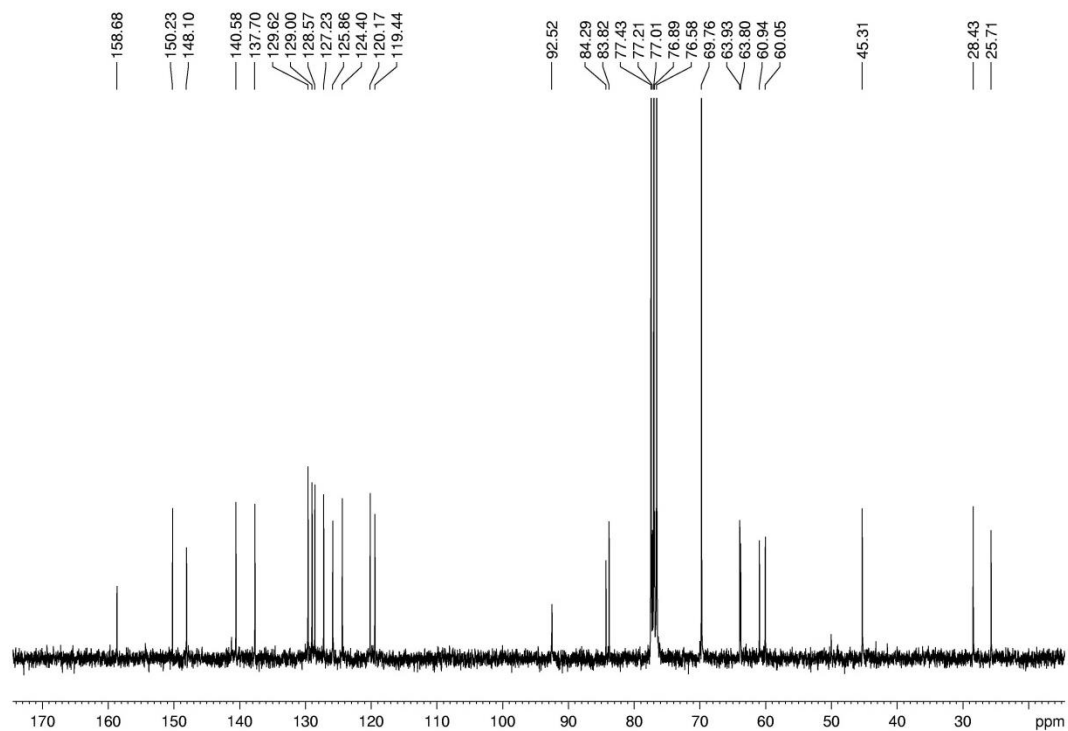


^1H and ^{13}C spectra for **188k**.

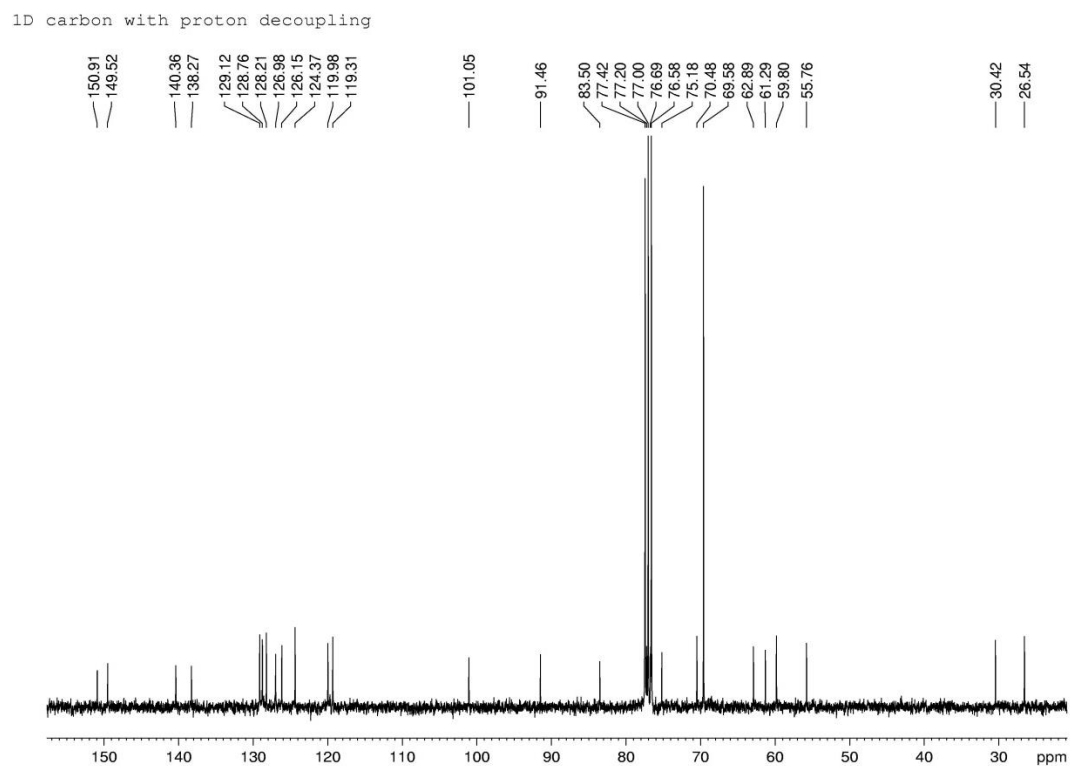
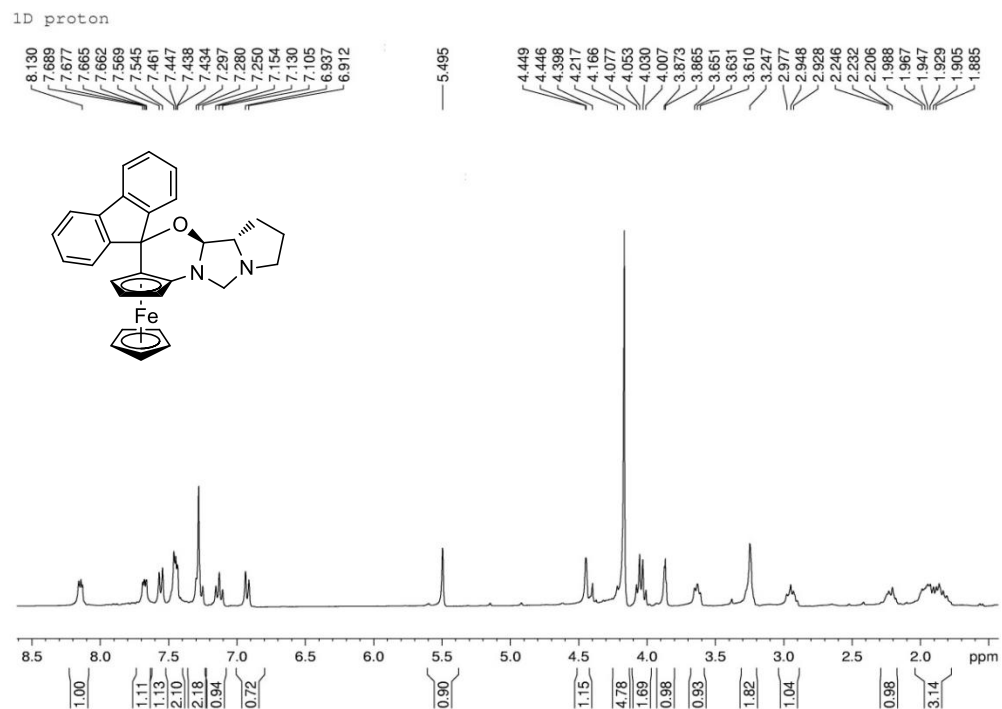
1D proton



1D carbon with proton decoupling

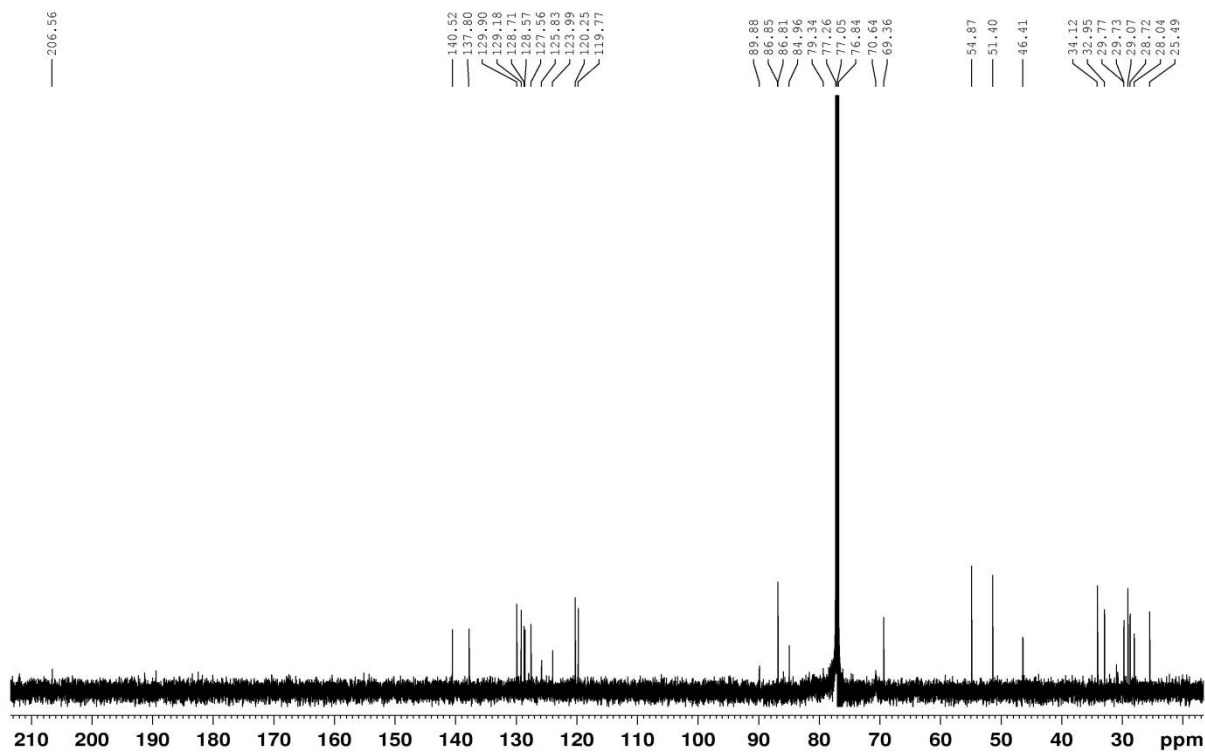


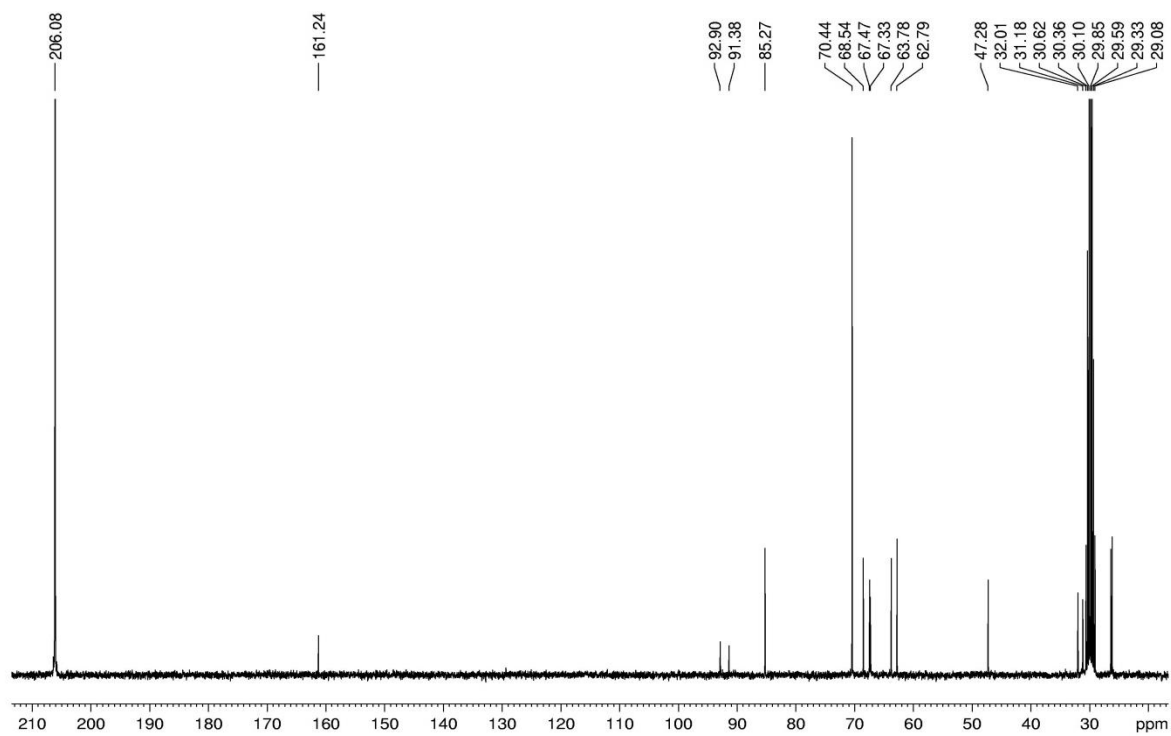
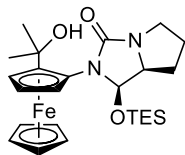
^1H , ^{13}C and nOe spectra for **211**.



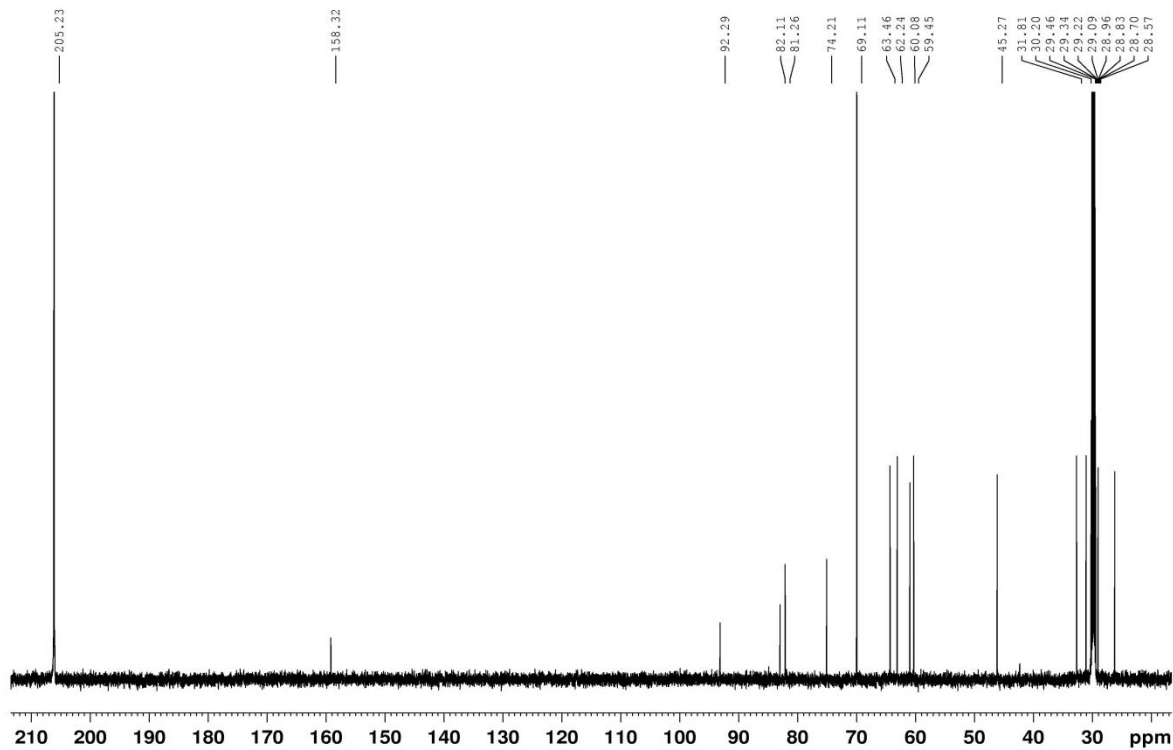
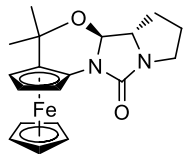
^1H and ^{13}C spectra for **212**.

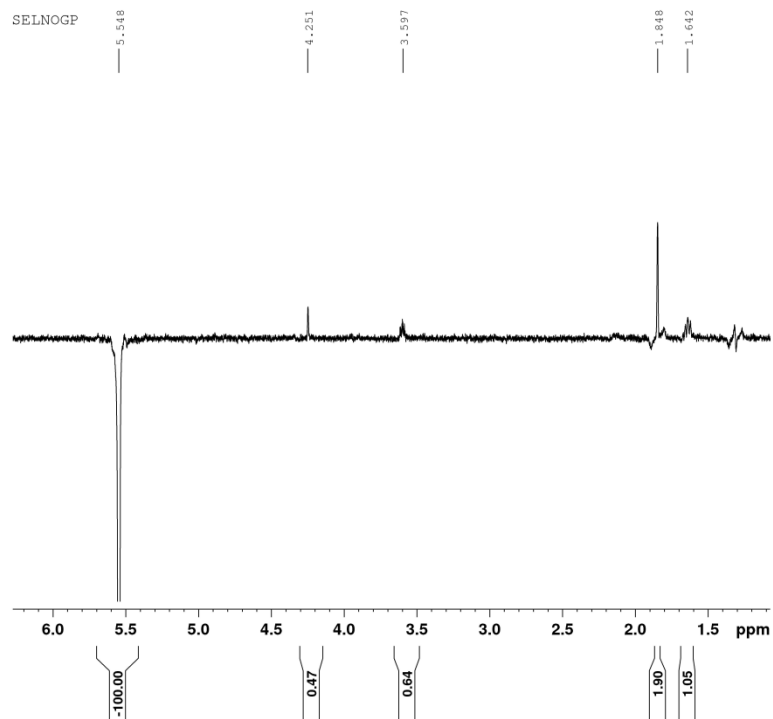
Chemical structure of compound 10: C1=CC=C(C=C1)C2=CC=CC=C2C3=CC=CC=C3C4=CC=CC=C4C5=CC=CC=C5C6=CC=CC=C6C7=CC=CC=C7C8=CC=CC=C8C9=CC=CC=C9C10=CC=CC=C10C11=CC=CC=C11C12=CC=CC=C12C13=CC=CC=C13C14=CC=CC=C14C15=CC=CC=C15C16=CC=CC=C16C17=CC=CC=C17C18=CC=CC=C18C19=CC=CC=C19C20=CC=CC=C20C21=CC=CC=C21C22=CC=CC=C22C23=CC=CC=C23C24=CC=CC=C24C25=CC=CC=C25C26=CC=CC=C26C27=CC=CC=C27C28=CC=CC=C28C29=CC=CC=C29C30=CC=CC=C30C31=CC=CC=C31C32=CC=CC=C32C33=CC=CC=C33C34=CC=CC=C34C35=CC=CC=C35C36=CC=CC=C36C37=CC=CC=C37C38=CC=CC=C38C39=CC=CC=C39C40=CC=CC=C40C41=CC=CC=C41C42=CC=CC=C42C43=CC=CC=C43C44=CC=CC=C44C45=CC=CC=C45C46=CC=CC=C46C47=CC=CC=C47C48=CC=CC=C48C49=CC=CC=C49C50=CC=CC=C50C51=CC=CC=C51C52=CC=CC=C52C53=CC=CC=C53C54=CC=CC=C54C55=CC=CC=C55C56=CC=CC=C56C57=CC=CC=C57C58=CC=CC=C58C59=CC=CC=C59C60=CC=CC=C60C61=CC=CC=C61C62=CC=CC=C62C63=CC=CC=C63C64=CC=CC=C64C65=CC=CC=C65C66=CC=CC=C66C67=CC=CC=C67C68=CC=CC=C68C69=CC=CC=C69C70=CC=CC=C70C71=CC=CC=C71C72=CC=CC=C72C73=CC=CC=C73C74=CC=CC=C74C75=CC=CC=C75C76=CC=CC=C76C77=CC=CC=C77C78=CC=CC=C78C79=CC=CC=C79C80=CC=CC=C80C81=CC=CC=C81C82=CC=CC=C82C83=CC=CC=C83C84=CC=CC=C84C85=CC=CC=C85C86=CC=CC=C86C87=CC=CC=C87C88=CC=CC=C88C89=CC=CC=C89C90=CC=CC=C90C91=CC=CC=C91C92=CC=CC=C92C93=CC=CC=C93C94=CC=CC=C94C95=CC=CC=C95C96=CC=CC=C96C97=CC=CC=C97C98=CC=CC=C98C99=CC=CC=C99C100=CC=CC=C100C101=CC=CC=C101C102=CC=CC=C102C103=CC=CC=C103C104=CC=CC=C104C105=CC=CC=C105C106=CC=CC=C106C107=CC=CC=C107C108=CC=CC=C108C109=CC=CC=C109C110=CC=CC=C110C111=CC=CC=C111C112=CC=CC=C112C113=CC=CC=C113C114=CC=CC=C114C115=CC=CC=C115C116=CC=CC=C116C117=CC=CC=C117C118=CC=CC=C118C119=CC=CC=C119C120=CC=CC=C120C121=CC=CC=C121C122=CC=CC=C122C123=CC=CC=C123C124=CC=CC=C124C125=CC=CC=C125C126=CC=CC=C126C127=CC=CC=C127C128=CC=CC=C128C129=CC=CC=C129C130=CC=CC=C130C131=CC=CC=C131C132=CC=CC=C132C133=CC=CC=C133C134=CC=CC=C134C135=CC=CC=C135C136=CC=CC=C136C137=CC=CC=C137C138=CC=CC=C138C139=CC=CC=C139C140=CC=CC=C140C141=CC=CC=C141C142=CC=CC=C142C143=CC=CC=C143C144=CC=CC=C144C145=CC=CC=C145C146=CC=CC=C146C147=CC=CC=C147C148=CC=CC=C148C149=CC=CC=C149C150=CC=CC=C150C151=CC=CC=C151C152=CC=CC=C152C153=CC=CC=C153C154=CC=CC=C154C155=CC=CC=C155C156=CC=CC=C156C157=CC=CC=C157C158=CC=CC=C158C159=CC=CC=C159C160=CC=CC=C160C161=CC=CC=C161C162=CC=CC=C162C163=CC=CC=C163C164=CC=CC=C164C165=CC=CC=C165C166=CC=CC=C166C167=CC=CC=C167C168=CC=CC=C168C169=CC=CC=C169C170=CC=CC=C170C171=CC=CC=C171C172=CC=CC=C172C173=CC=CC=C173C174=CC=CC=C174C175=CC=CC=C175C176=CC=CC=C176C177=CC=CC=C177C178=CC=CC=C178C179=CC=CC=C179C180=CC=CC=C180C181=CC=CC=C181C182=CC=CC=C182C183=CC=CC=C183C184=CC=CC=C184C185=CC=CC=C185C186=CC=CC=C186C187=CC=CC=C187C188=CC=CC=C188C189=CC=CC=C189C190=CC=CC=C190C191=CC=CC=C191C192=CC=CC=C192C193=CC=CC=C193C194=CC=CC=C194C195=CC=CC=C195C196=CC=CC=C196C197=CC=CC=C197C198=CC=CC=C198C199=CC=CC=C199C200=CC=CC=C200C201=CC=CC=C201C202=CC=CC=C202C203=CC=CC=C203C204=CC=CC=C204C205=CC=CC=C205C206=CC=CC=C206C207=CC=CC=C207C208=CC=CC=C208C209=CC=CC=C209C210=CC=CC=C210C211=CC=CC=C211C212=CC=CC=C212C213=CC=CC=C213C214=CC=CC=C214C215=CC=CC=C215C216=CC=CC=C216C217=CC=CC=C217C218=CC=CC=C218C219=CC=CC=C219C220=CC=CC=C220C221=CC=CC=C221C222=CC=CC=C222C223=CC=CC=C223C224=CC=CC=C224C225=CC=CC=C225C226=CC=CC=C226C227=CC=CC=C227C228=CC=CC=C228C229=CC=CC=C229C230=CC=CC=C230C231=CC=CC=C231C232=CC=CC=C232C233=CC=CC=C233C234=CC=CC=C234C235=CC=CC=C235C236=CC=CC=C236C237=CC=CC=C237C238=CC=CC=C238C239=CC=CC=C239C240=CC=CC=C240C241=CC=CC=C241C242=CC=CC=C242C243=CC=CC=C243C244=CC=CC=C244C245=CC=CC=C245C246=CC=CC=C246C247=CC=CC=C247C248=CC=CC=C248C249=CC=CC=C249C250=CC=CC=C250C251=CC=CC=C251C252=CC=CC=C252C253=CC=CC=C253C254=CC=CC=C254C255=CC=CC=C255C256=CC=CC=C256C257=CC=CC=C257C258=CC=CC=C258C259=CC=CC=C259C260=CC=CC=C260C261=CC=CC=C261C262=CC=CC=C262C263=CC=CC=C263C264=CC=CC=C264C265=CC=CC=C265C266=CC=CC=C266C267=CC=CC=C267C268=CC=CC=C268C269=CC=CC=C269C270=CC=CC=C270C271=CC=CC=C271C272=CC=CC=C272C273=CC=CC=C273C274=CC=CC=C274C275=CC=CC=C275C276=CC=CC=C276C277=CC=CC=C277C278=CC=CC=C278C279=CC=CC=C279C280=CC=CC=C280C281=CC=CC=C281C282=CC=CC=C282C283=CC=CC=C283C284=CC=CC=C284C285=CC=CC=C285C286=CC=CC=C286C287=CC=CC=C287C288=CC=CC=C288C289=CC=CC=C289C290=CC=CC=C290C291=CC=CC=C291C292=CC=CC=C292C293=CC=CC=C293C294=CC=CC=C294C295=CC=CC=C295C296=CC=CC=C296C297=CC=CC=C297C298=CC=CC=C298C299=CC=CC=C299C300=CC=CC=C300C301=CC=CC=C301C302=CC=CC=C302C303=CC=CC=C303C304=CC=CC=C304C305=CC=CC=C305C306=CC=CC=C306C307=CC=CC=C307C308=CC=CC=C308C309=CC=CC=C309C310=CC=CC=C310C311=CC=CC=C311C312=CC=CC=C312C313=CC=CC=C313C314=CC=CC=C314C315=CC=CC=C315C316=CC=CC=C316C317=CC=CC=C317C318=CC=CC=C318C319=CC=CC=C319C320=CC=CC=C320C321=CC=CC=C321C322=CC=CC=C322C323=CC=CC=C323C324=CC=CC=C324C325=CC=CC=C325C326=CC=CC=C326C327=CC=CC=C327C328=CC=CC=C328C329=CC=CC=C329C330=CC=CC=C330C331=CC=CC=C331C332=CC=CC=C332C333=CC=CC=C333C334=CC=CC=C334C335=CC=CC=C335C336=CC=CC=C336C337=CC=CC=C337C338

¹H and ¹³C spectra for **214**.



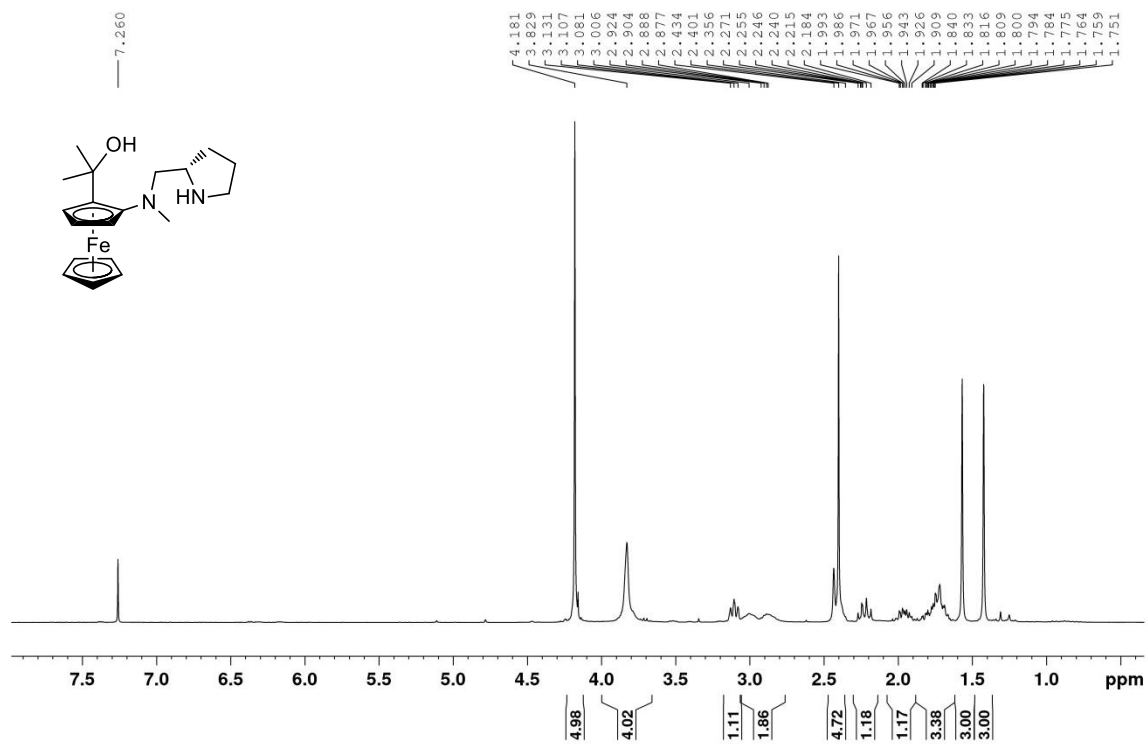
246



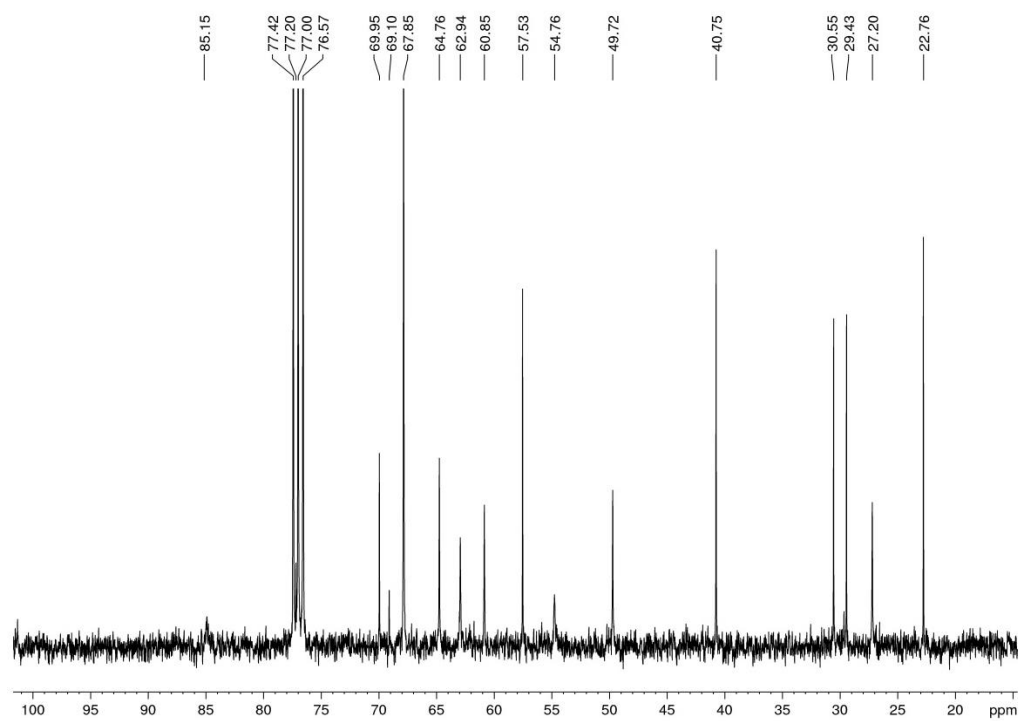


^1H , ^{13}C and nOe spectra for **215**.

1D proton

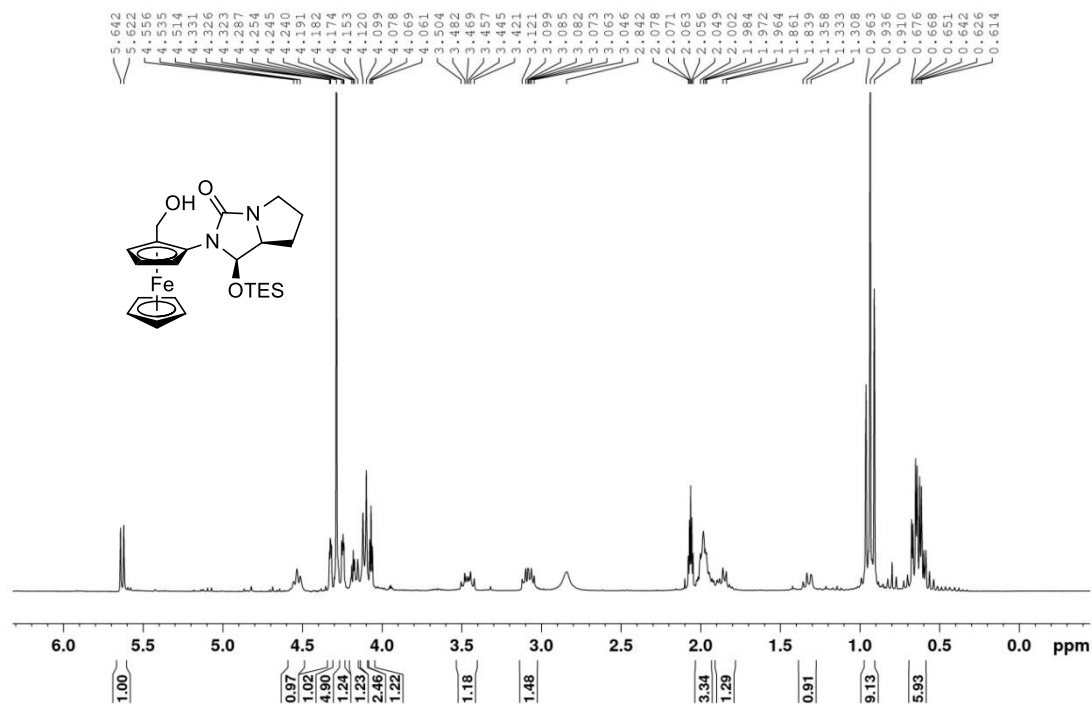


1D carbon with proton decoupling

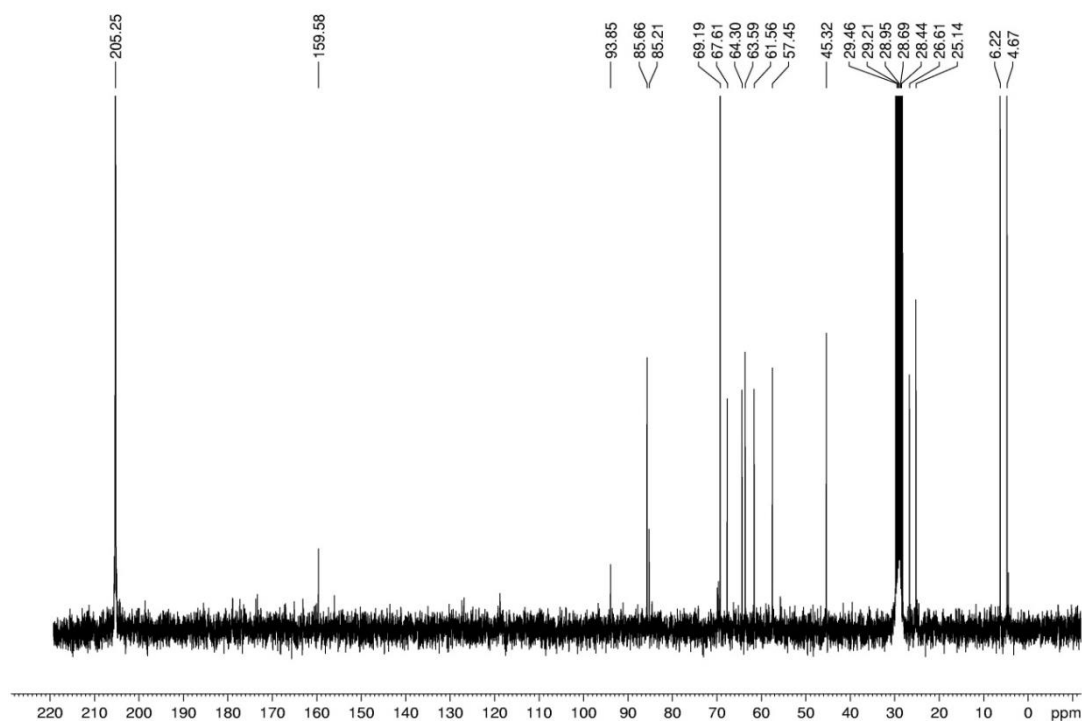


^1H and ^{13}C spectra for **216**.

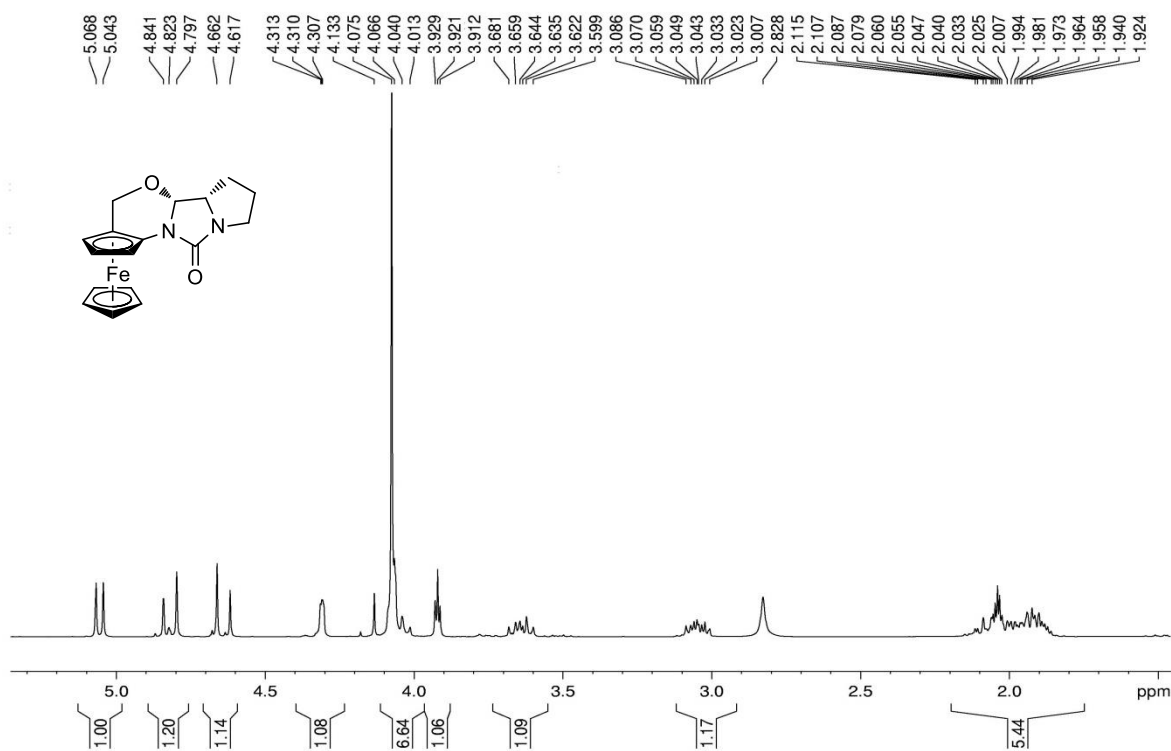
1D proton



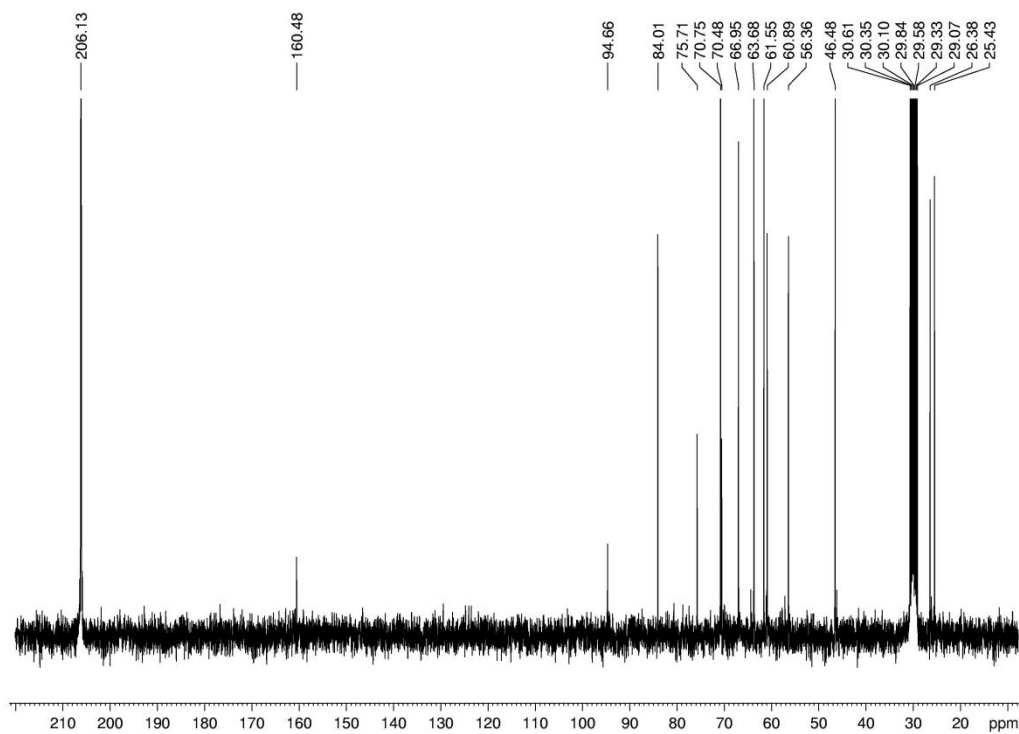
1D carbon with proton decoupling



^1H and ^{13}C spectra for **217**.

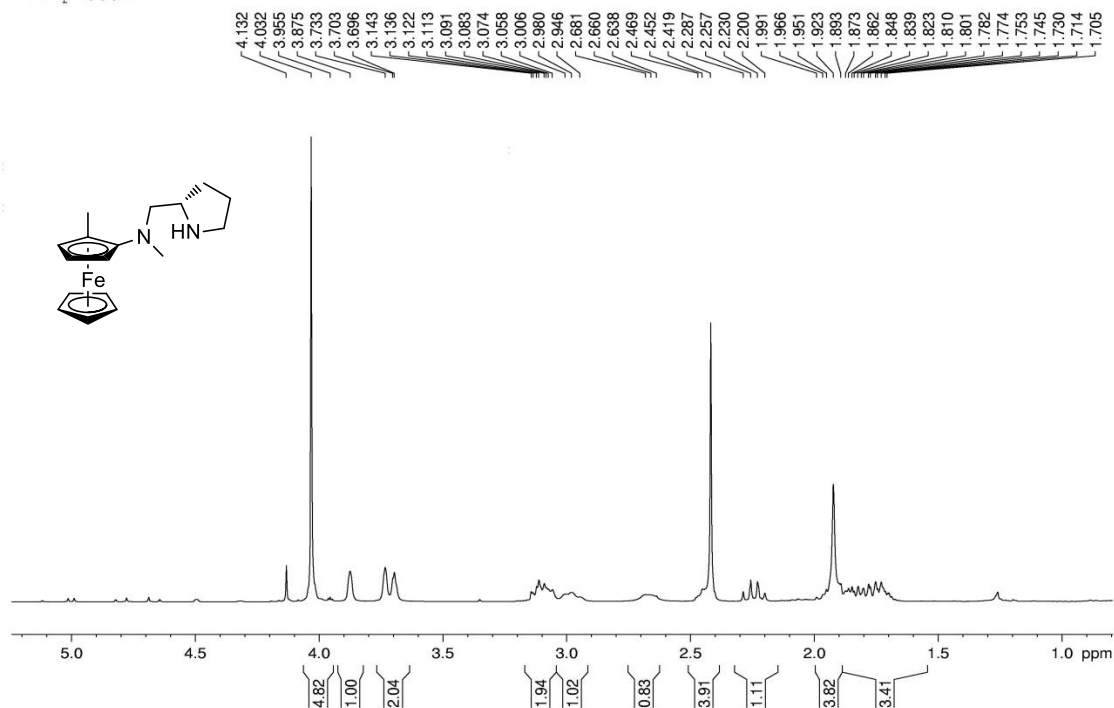


1D carbon with proton decoupling

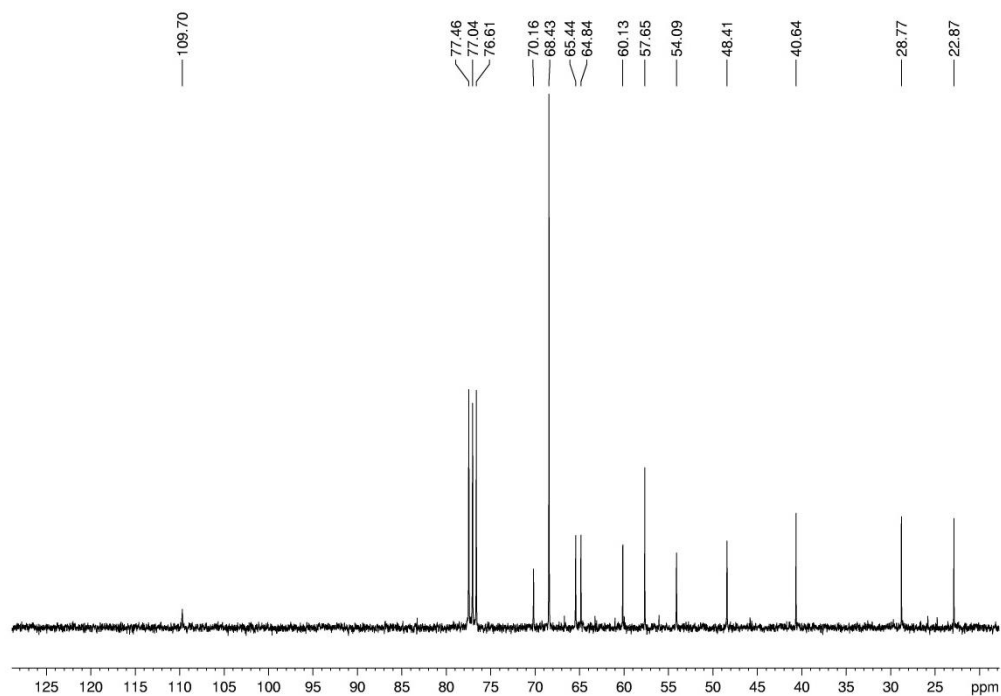


^1H and ^{13}C spectra for **218**.

1D proton

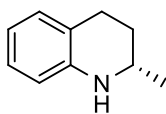
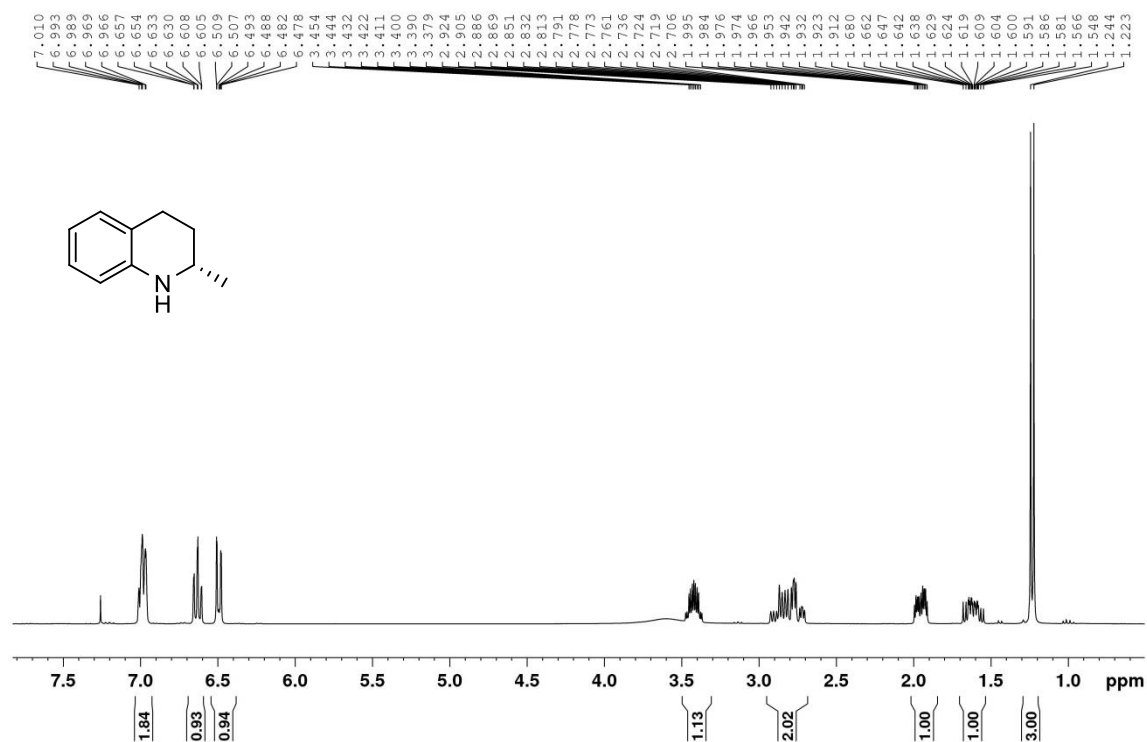


1D carbon with proton decoupling

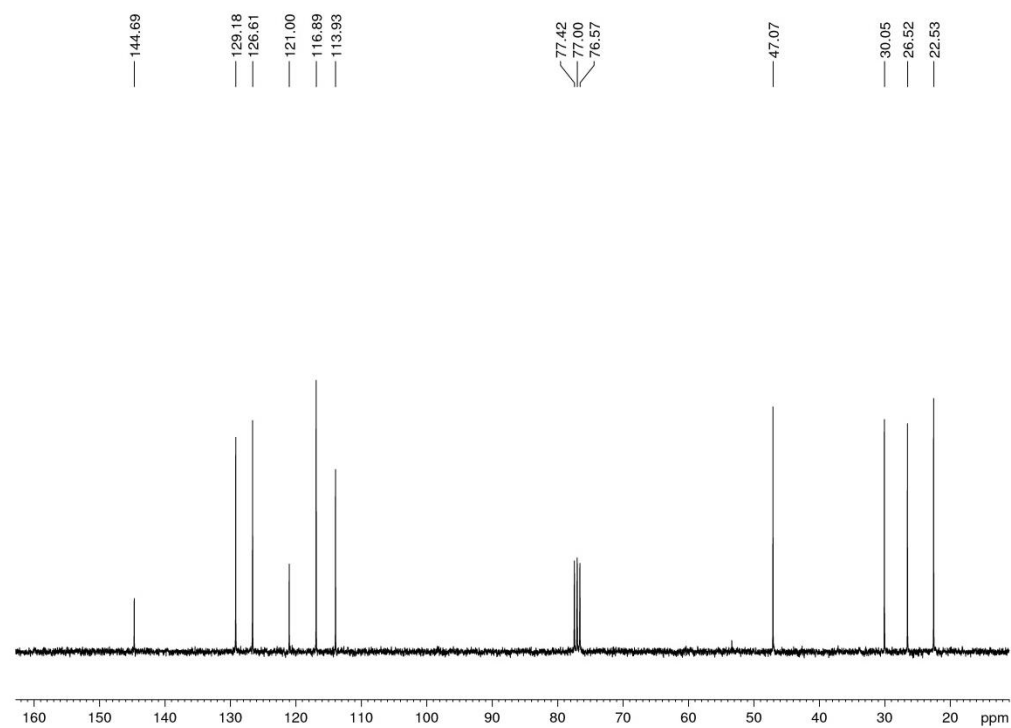


^1H and ^{13}C spectra for **219**.

1D proton

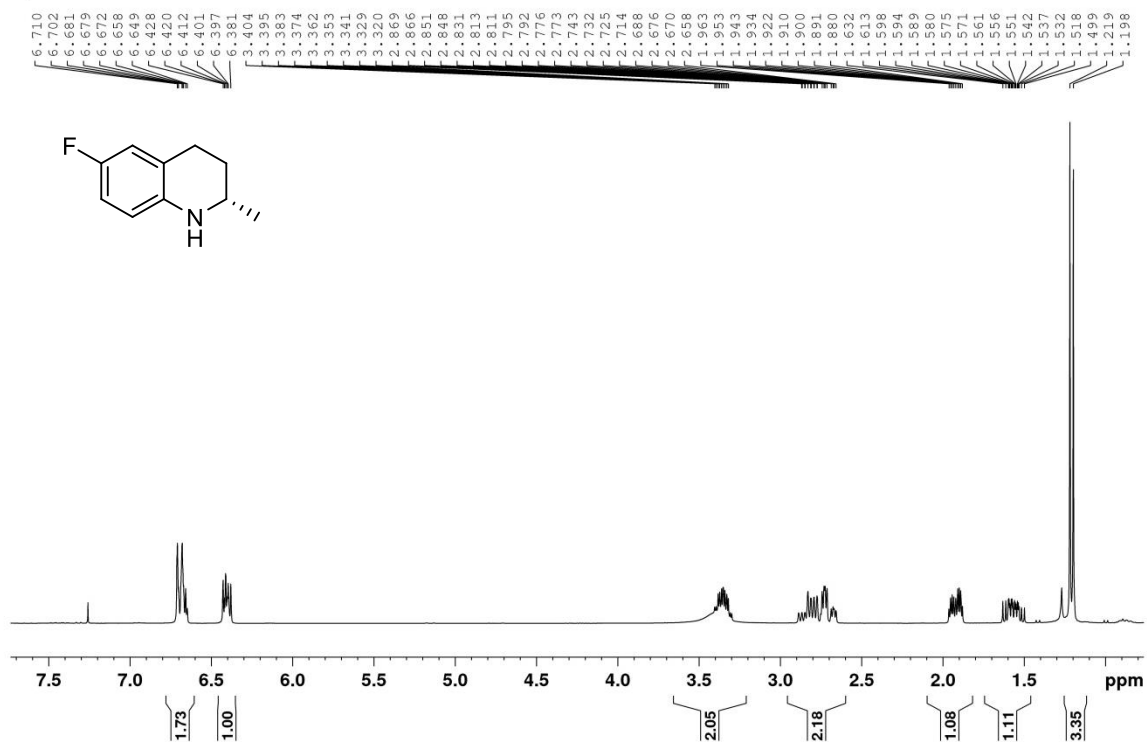


1D carbon with proton decoupling

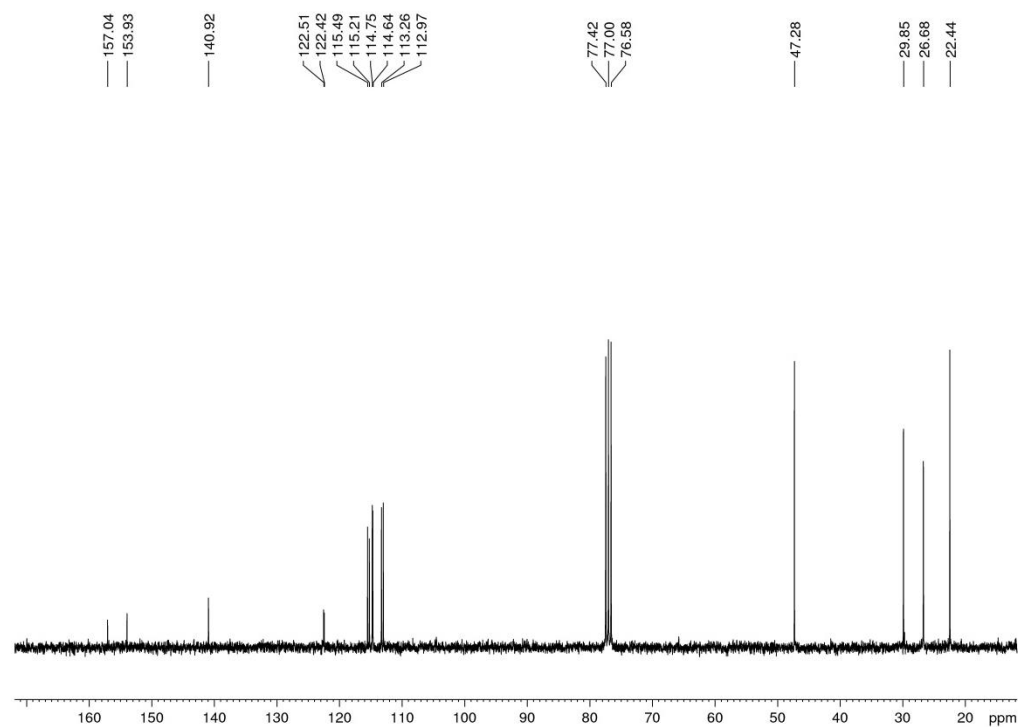


^1H and ^{13}C spectra for **203a**.

1D proton

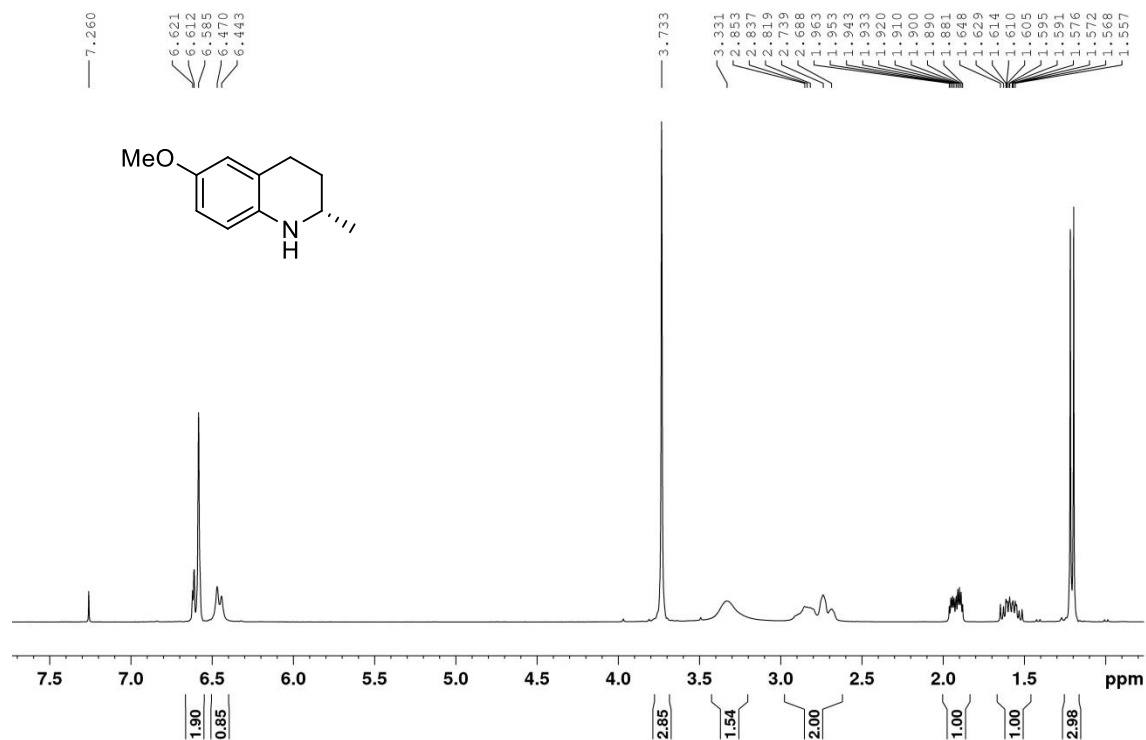


1D carbon with proton decoupling

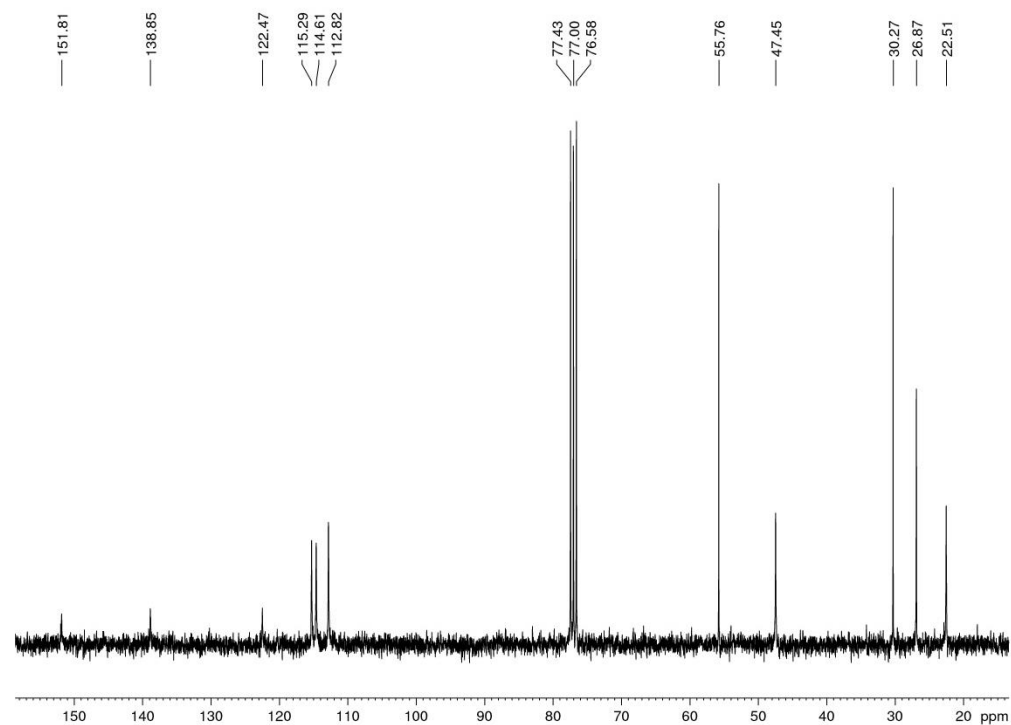


^1H and ^{13}C spectra for **203b**.

^1H proton

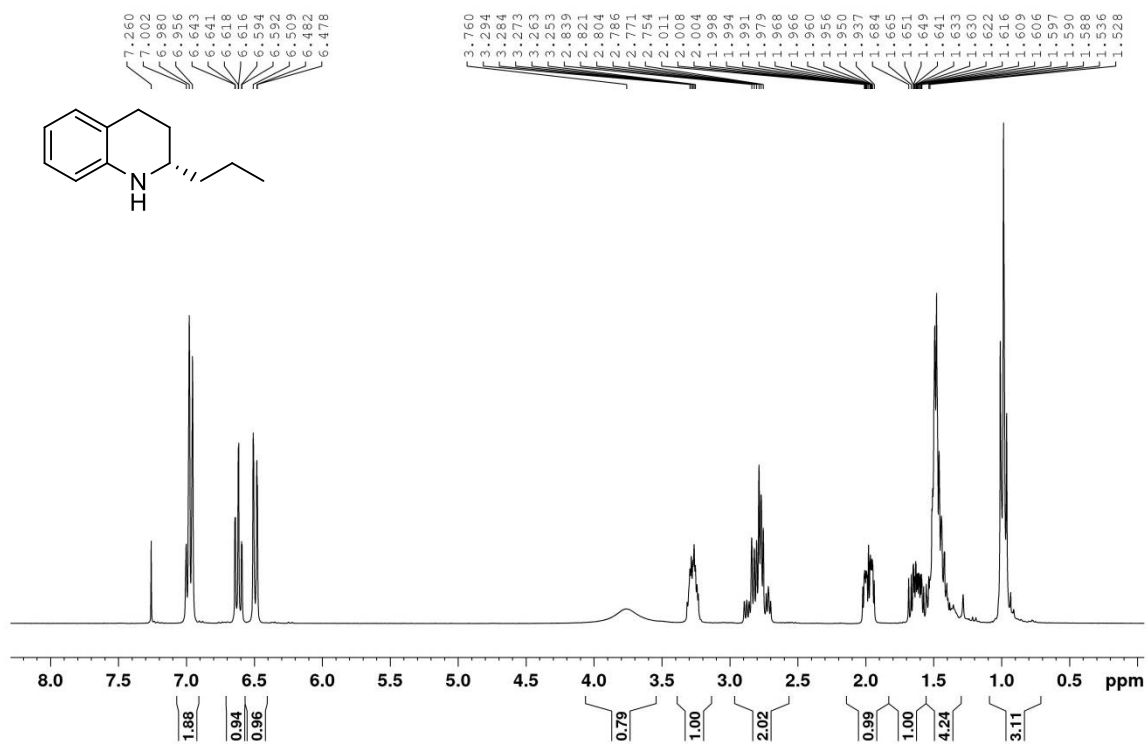


1D carbon with proton decoupling

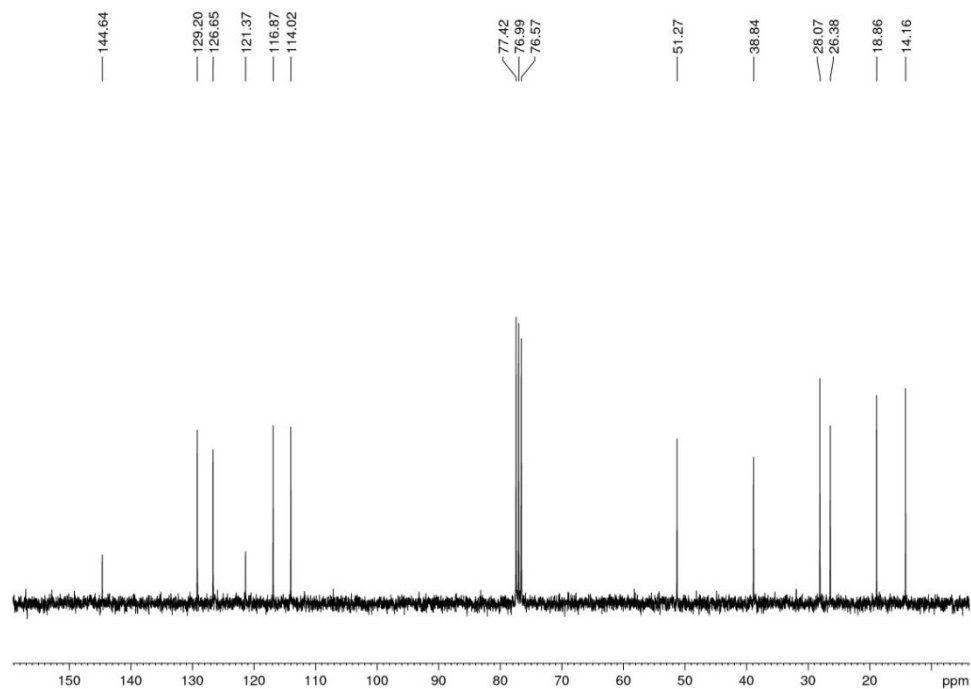


^1H and ^{13}C spectra for **203c**.

1D proton

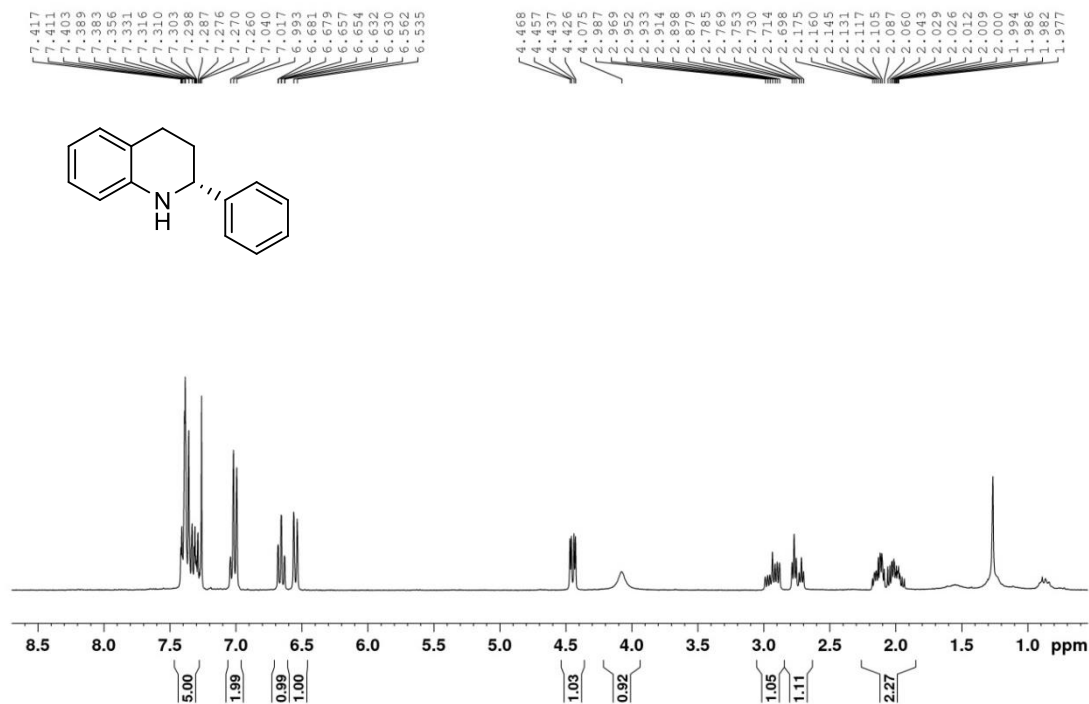


1D carbon with proton decoupling

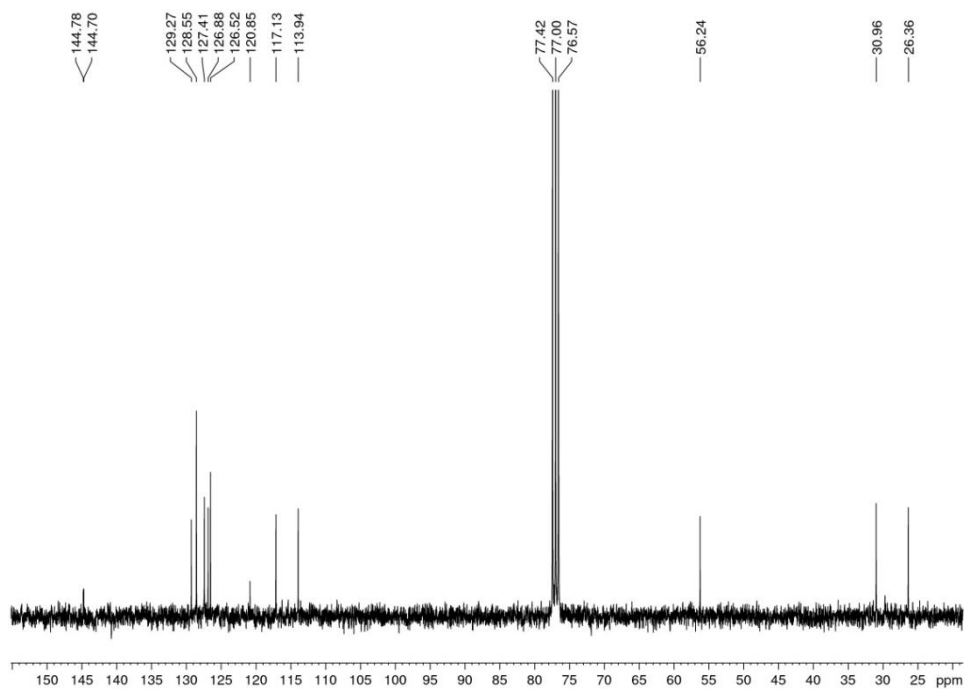


^1H and ^{13}C spectra for **203d**.

1D proton

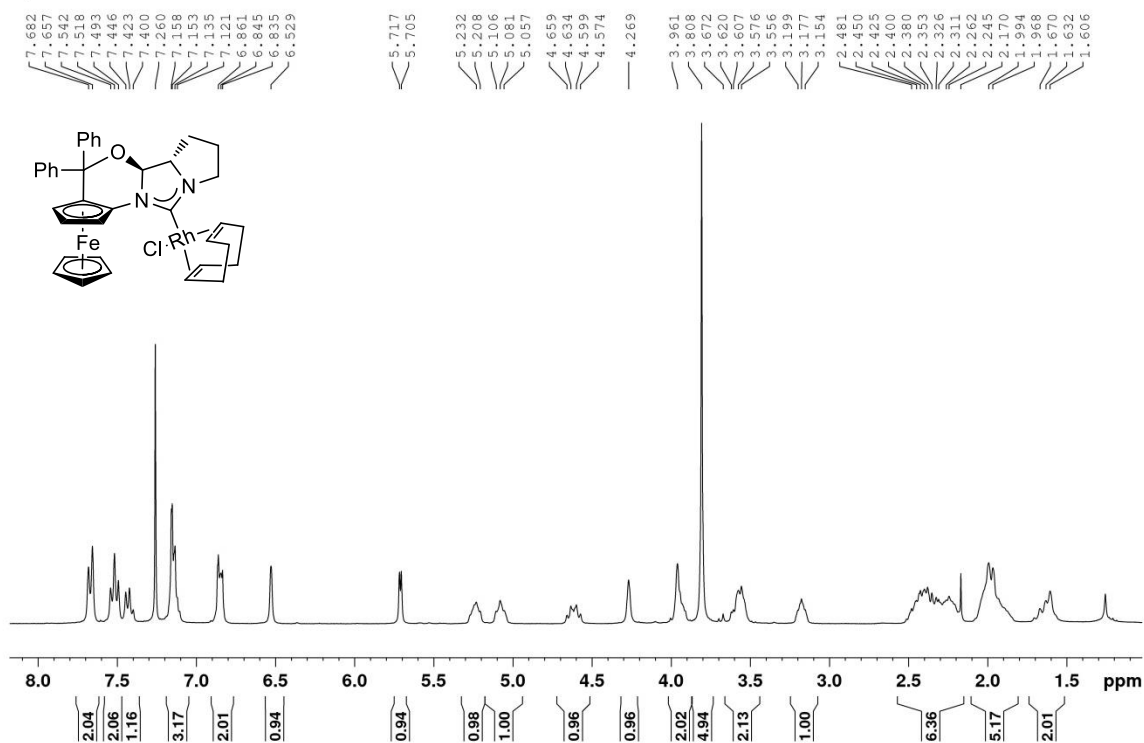


1D carbon with proton decoupling

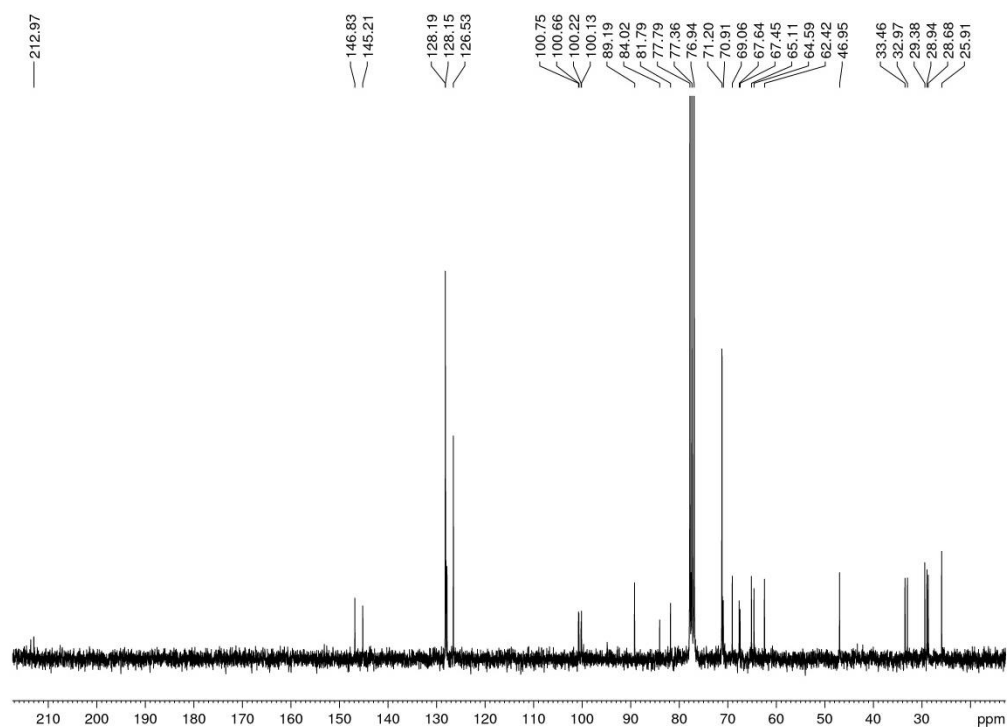


^1H and ^{13}C spectra for **203e**.

1D proton

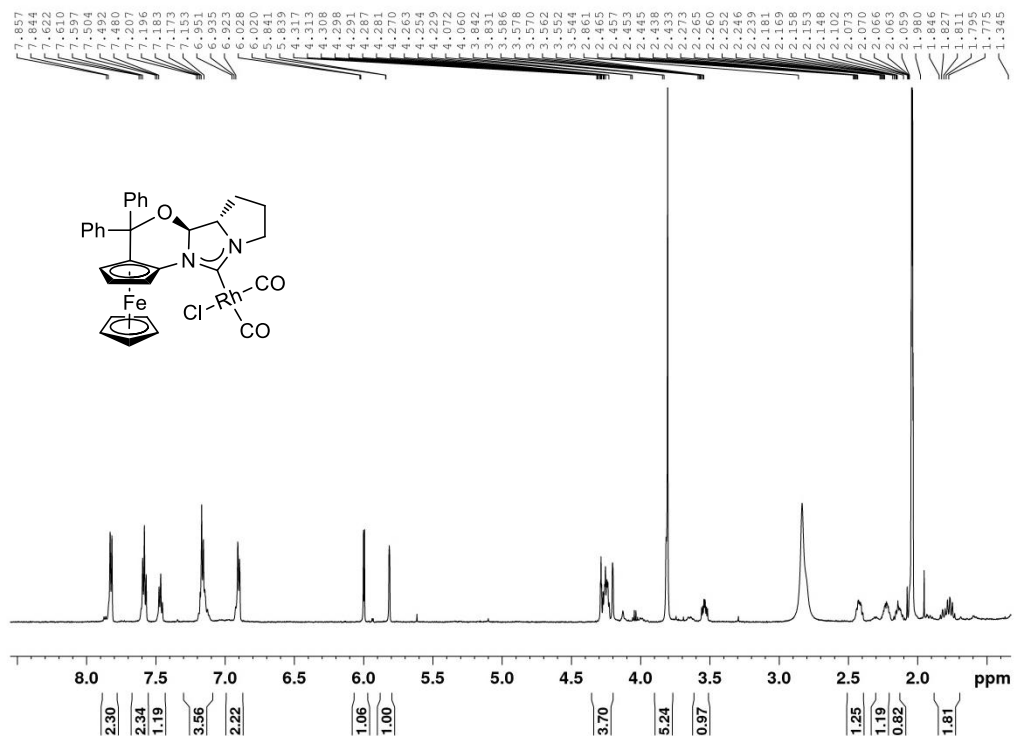


1D carbon with proton decoupling

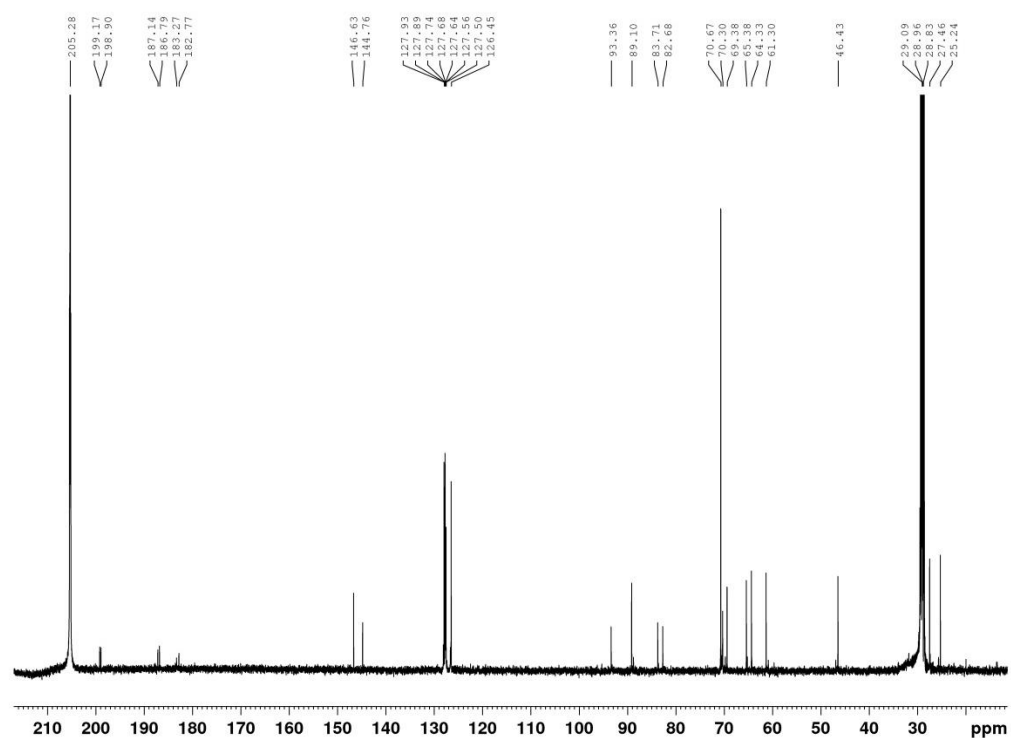


^1H and ^{13}C spectra for **226**.

1d proton

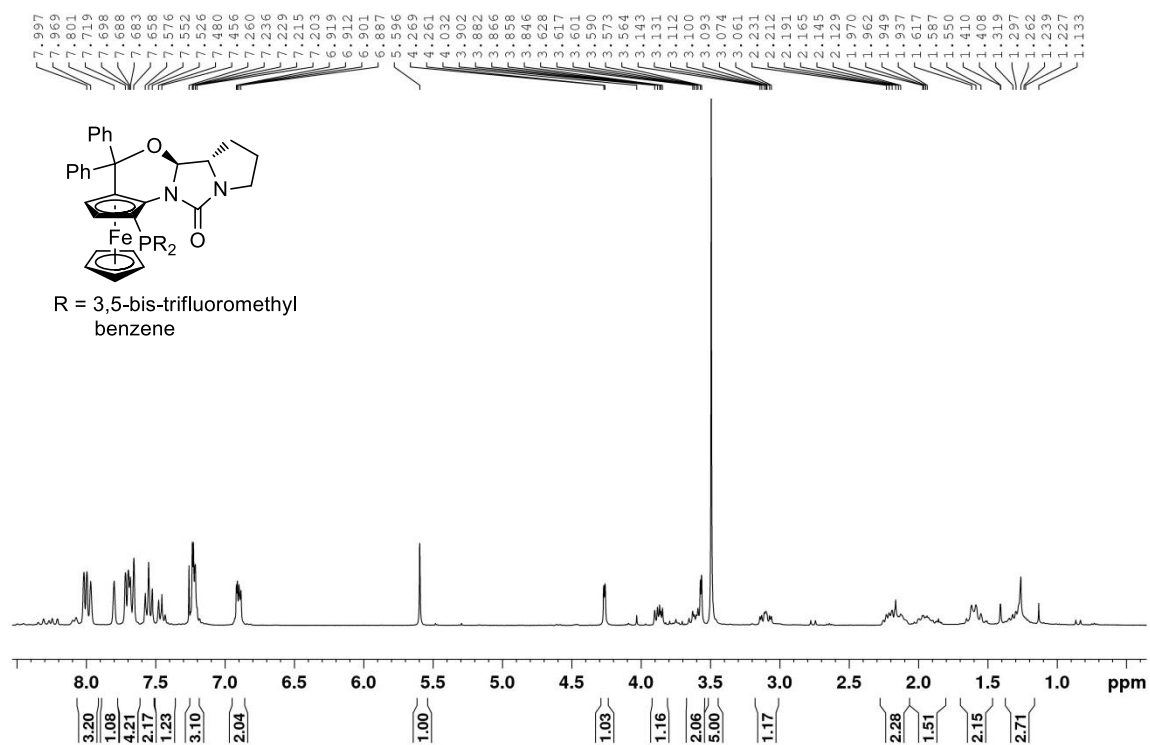


1d carbon with proton decoupling

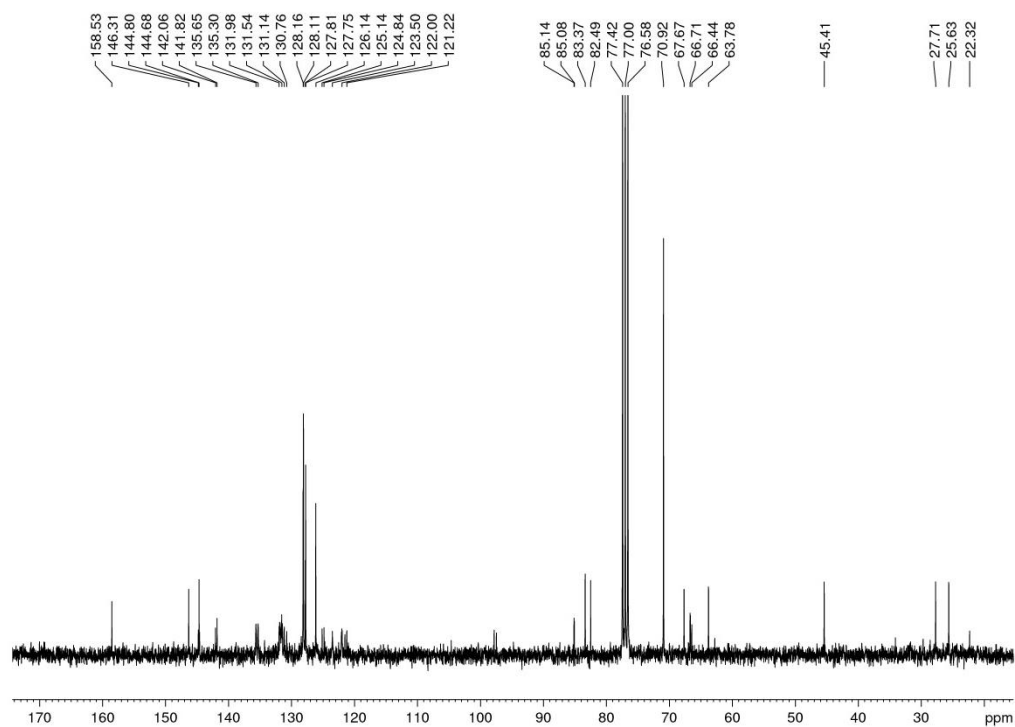


^1H and ^{13}C spectra for **227**.

1D proton

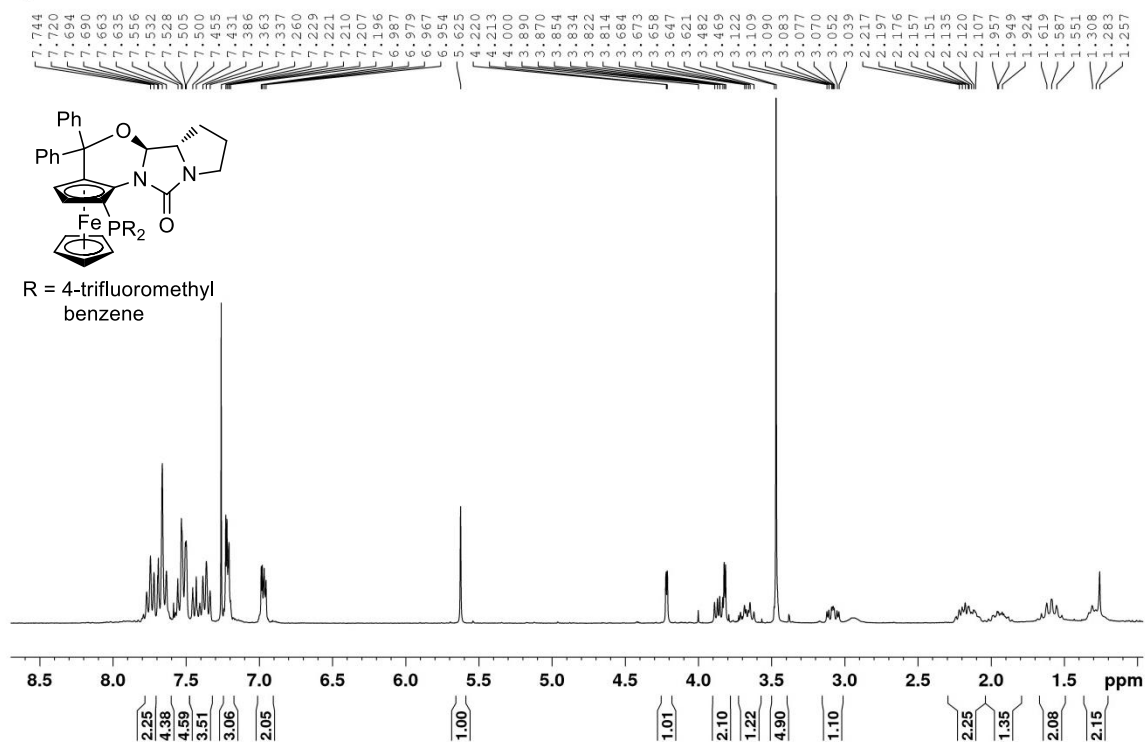


1D carbon with proton decoupling

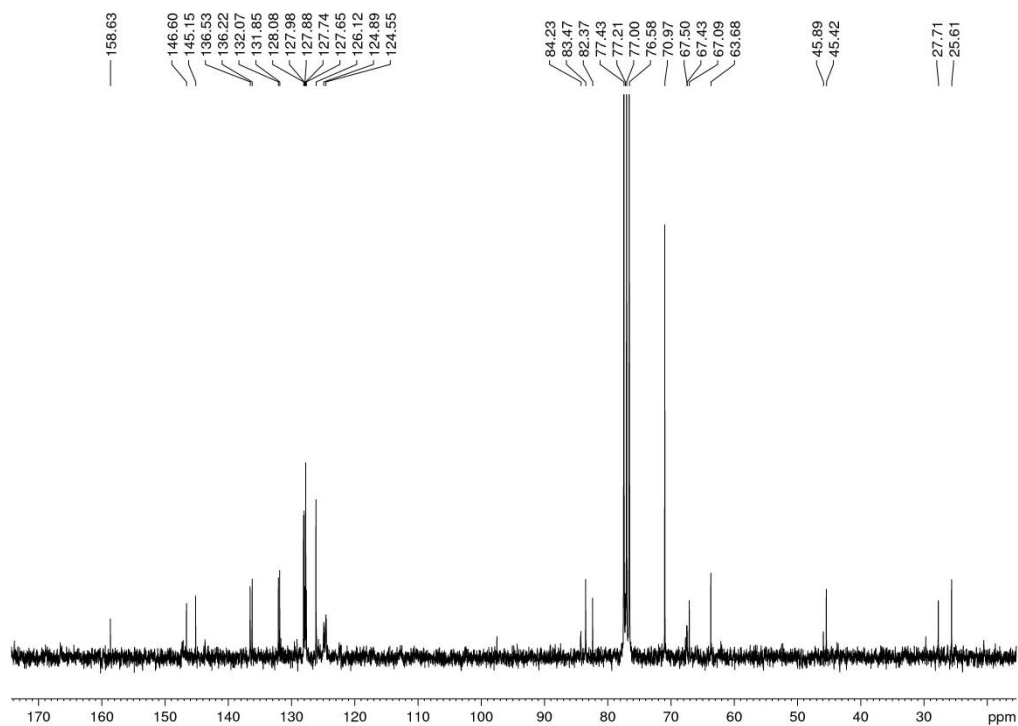


^1H and ^{13}C spectra for **220a**.

1D proton

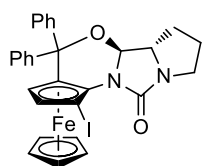
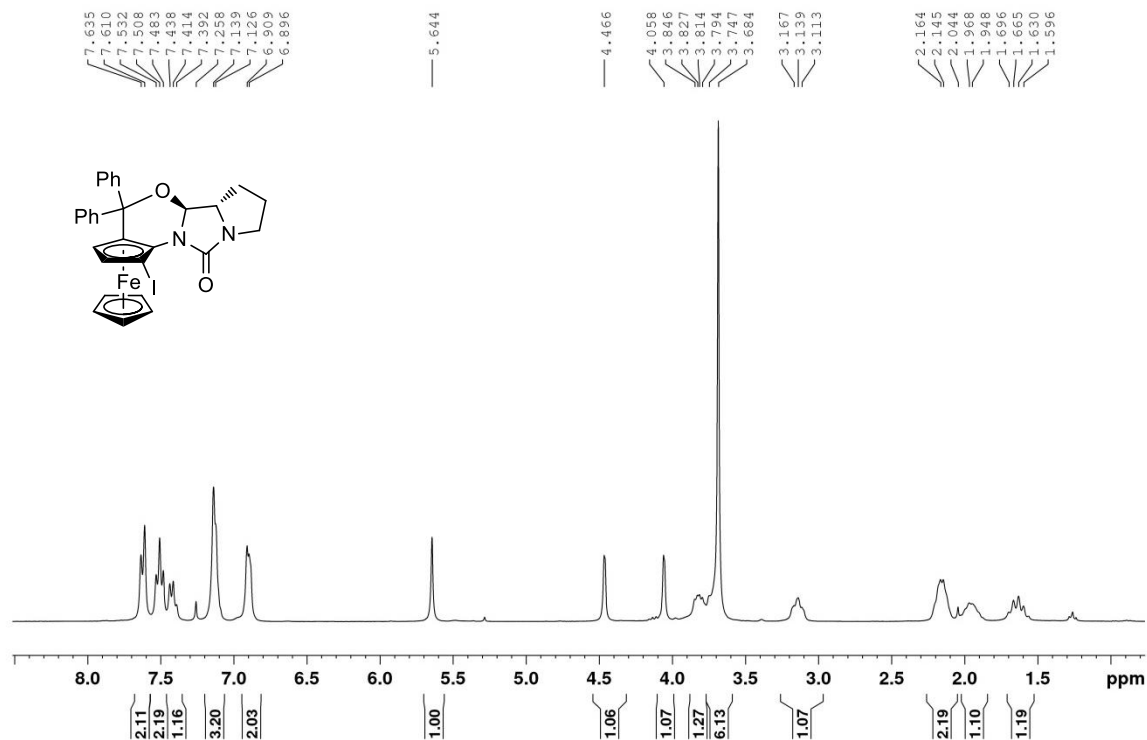


1D carbon with proton decoupling

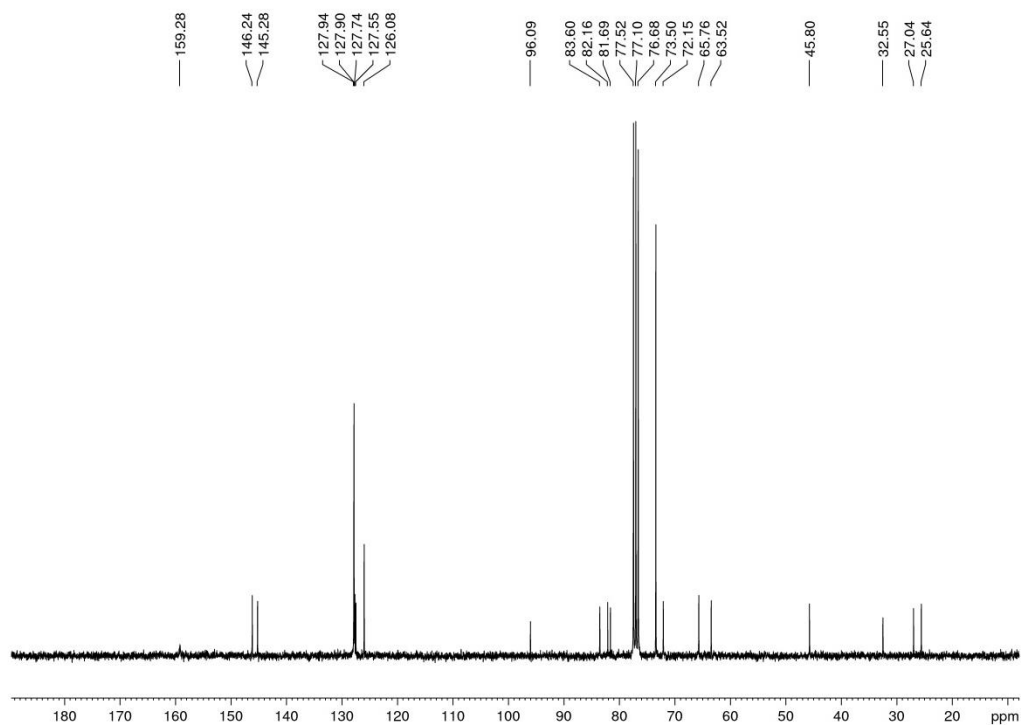


^1H and ^{13}C spectra for **220b**.

1D proton

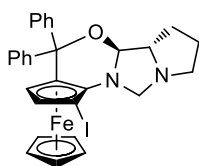
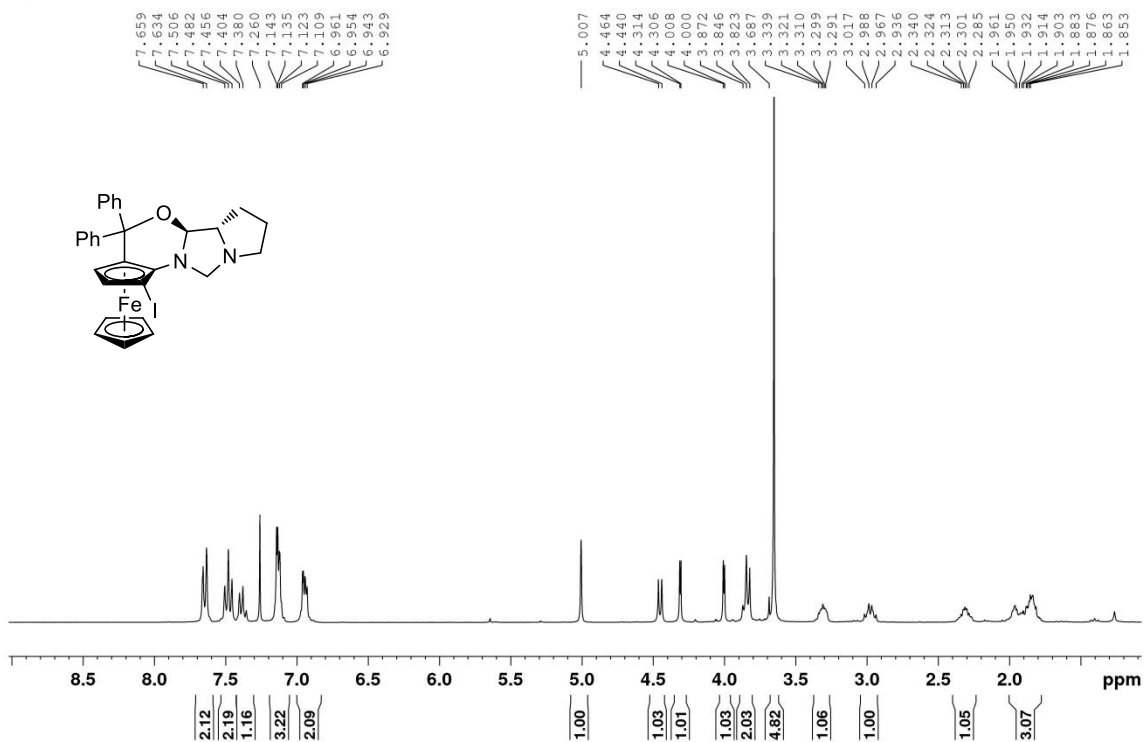


1D carbon with proton decoupling

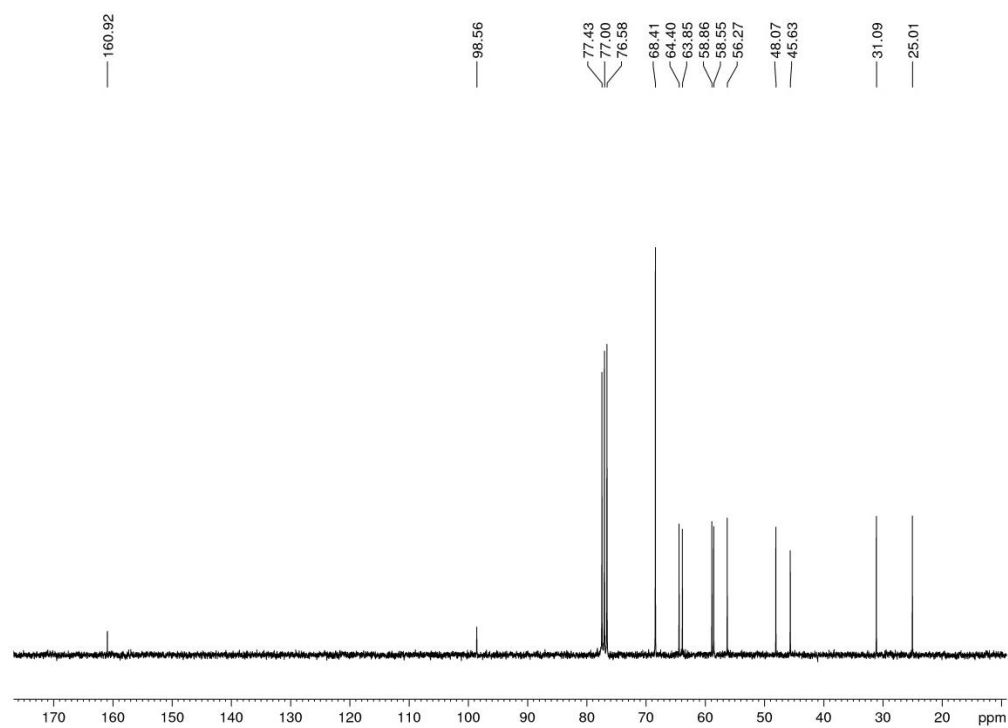


^1H and ^{13}C spectra for **221**.

1D proton

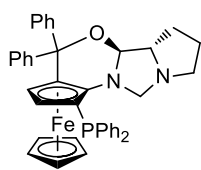
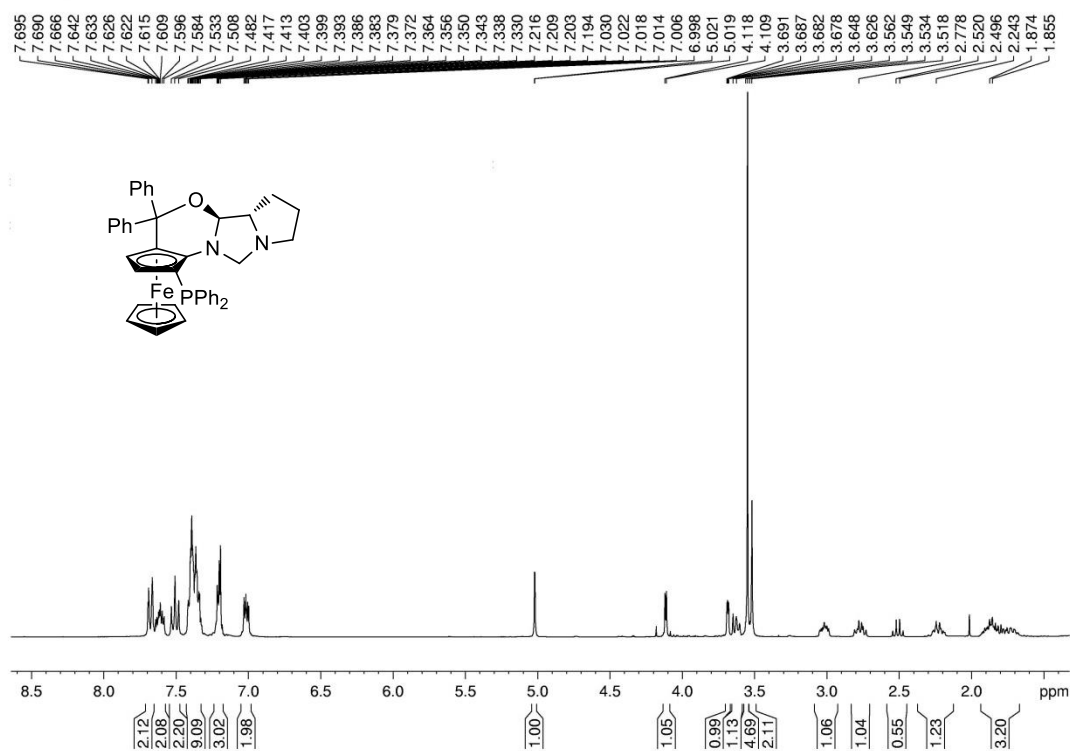


1D carbon with proton decoupling

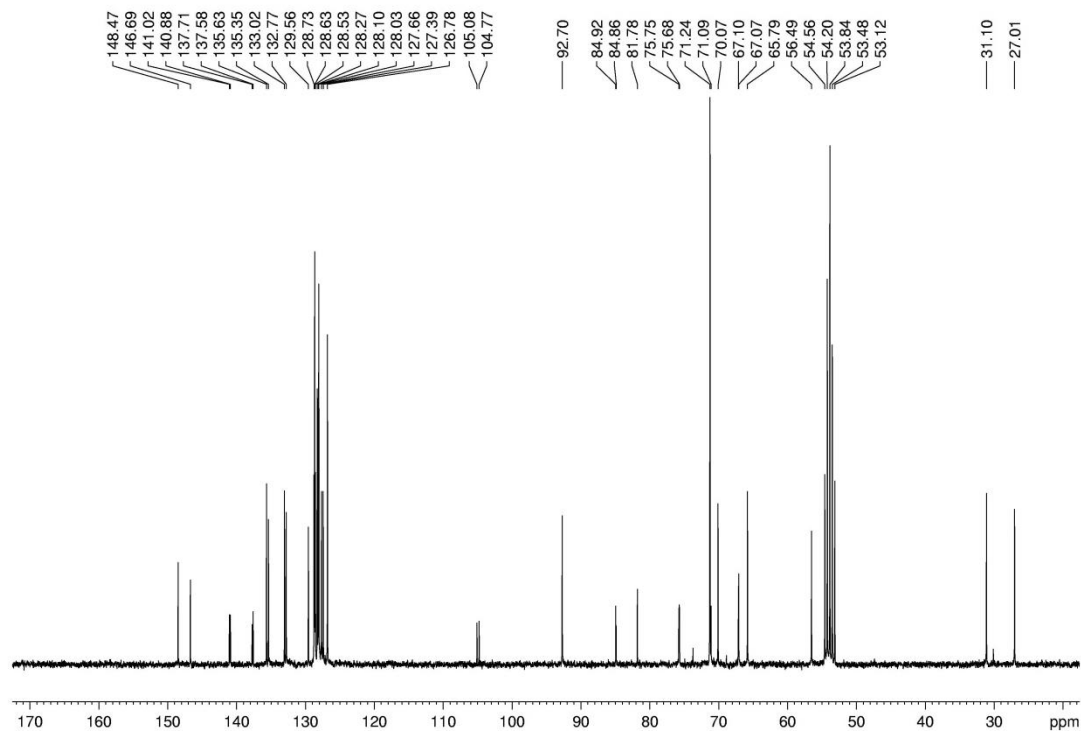


^1H and ^{13}C spectra for **222**.

1D proton

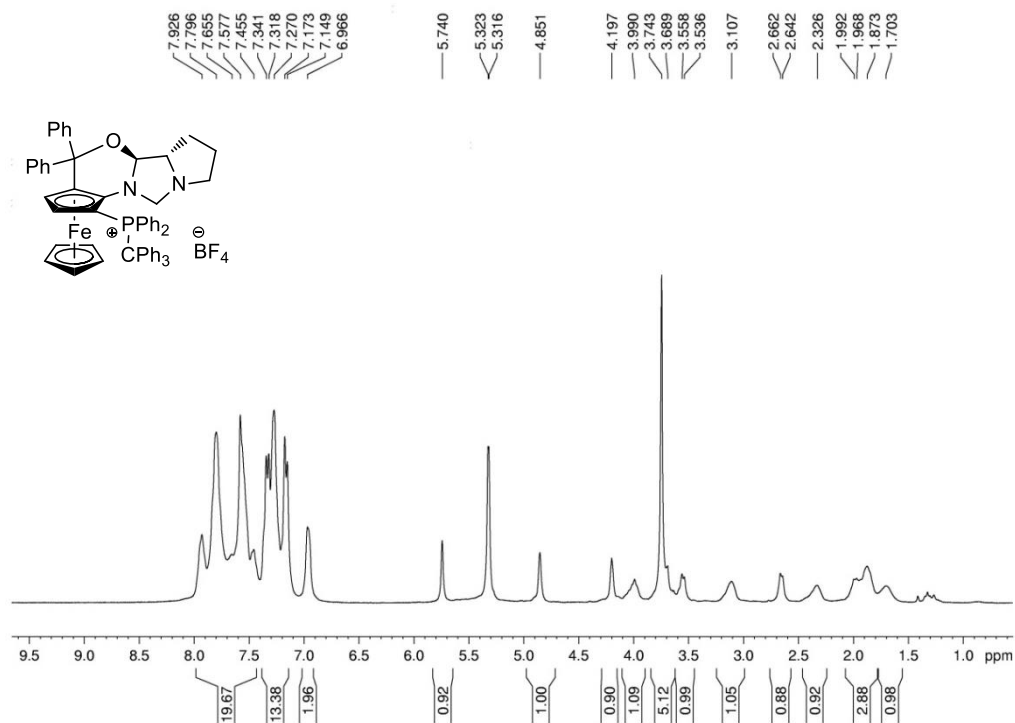


1D carbon with proton decoupling



^1H and ^{13}C spectra for **223**.

1D proton



1D proton

Chemical structure of the compound is shown:

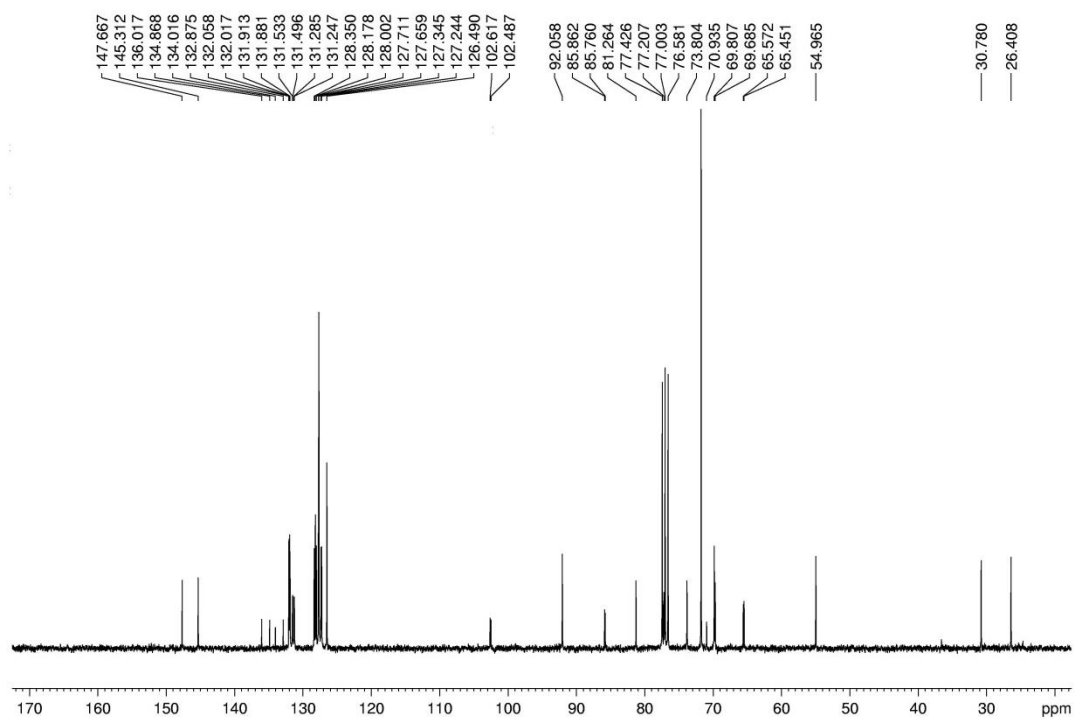
c1ccccc1C2(Cc3ccccc3)N(C2)c4ccccc4S(=S)(c5ccccc5)P(c6ccccc6)c7ccccc7

Peak list (ppm):

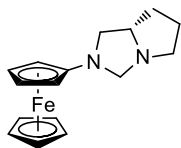
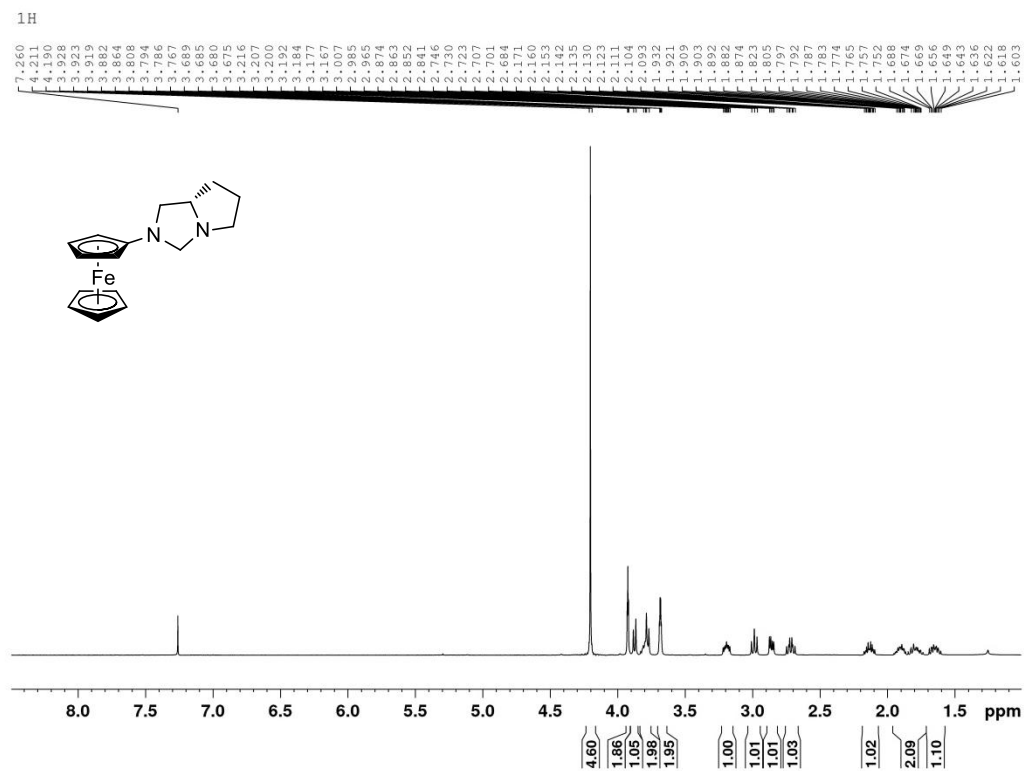
- 7.854, 7.834, 7.810, 7.715, 7.690, 7.529, 7.505, 7.480, 7.424, 7.399, 7.375, 7.260, 7.193, 7.182, 7.172, 6.997, 6.989, 6.978, 6.967
- 4.913
- 4.059, 4.054, 3.903, 3.880, 3.814, 3.735, 3.693, 3.425, 3.402
- 3.003, 2.984, 2.247, 2.222, 2.198, 2.174, 2.161, 1.911, 1.890, 1.875, 1.859, 1.840, 1.819, 1.800

Integration values (from left to right):

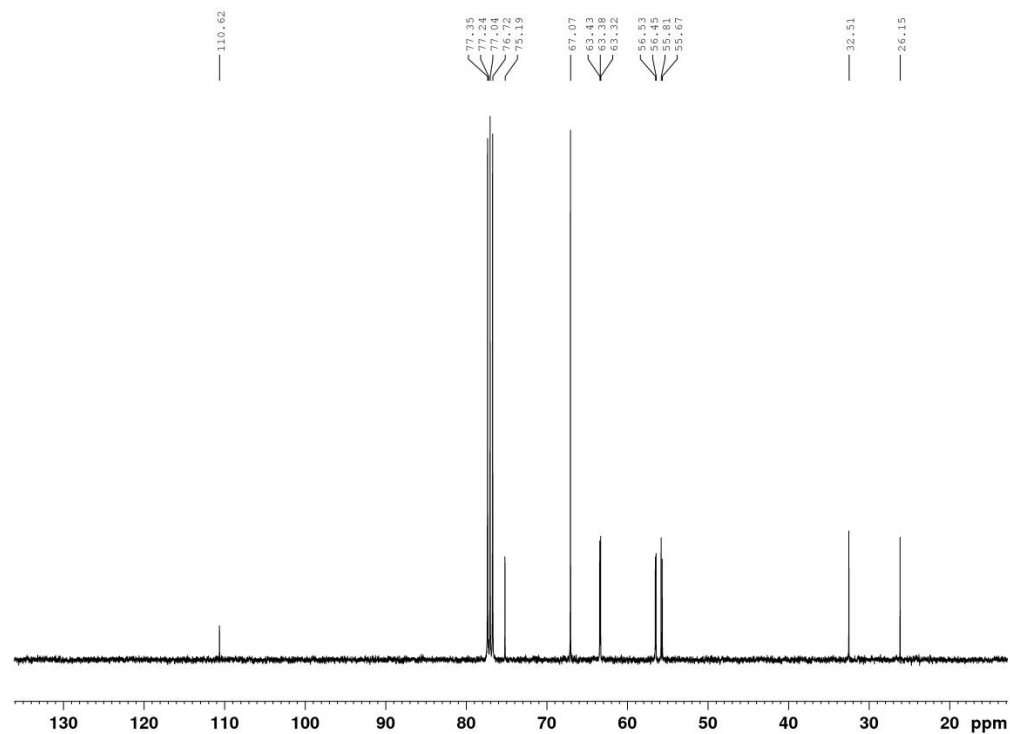
- 4.07, 2.03, 9.32, 3.10, 2.06
- 1.00
- 1.02, 1.18, 4.92, 2.12, 1.00
- 1.98
- 1.09, 3.33



¹H and ¹³C spectra for **225**.

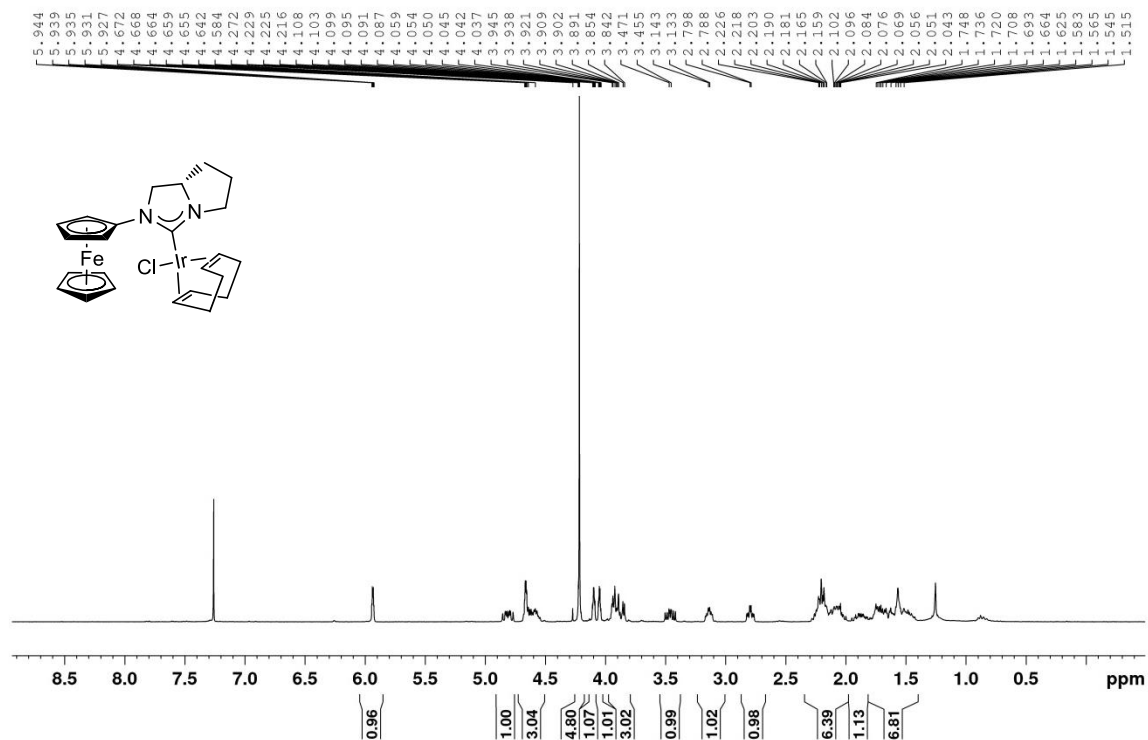


^{13}C with ^1H decoupling

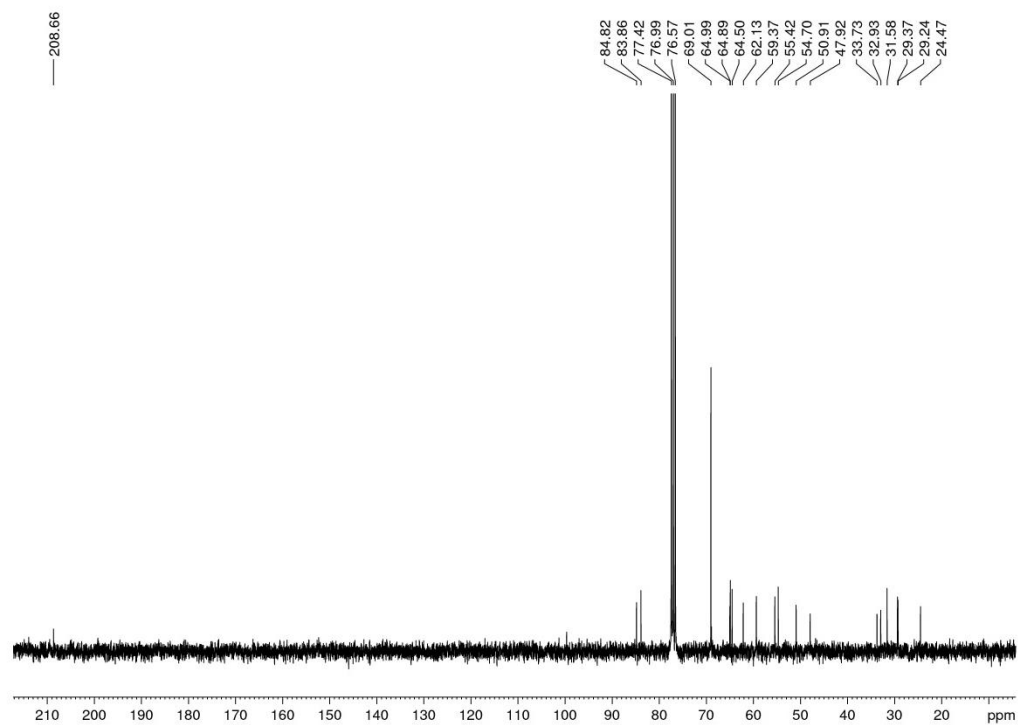


^1H and ^{13}C spectra for **228**.

1D proton

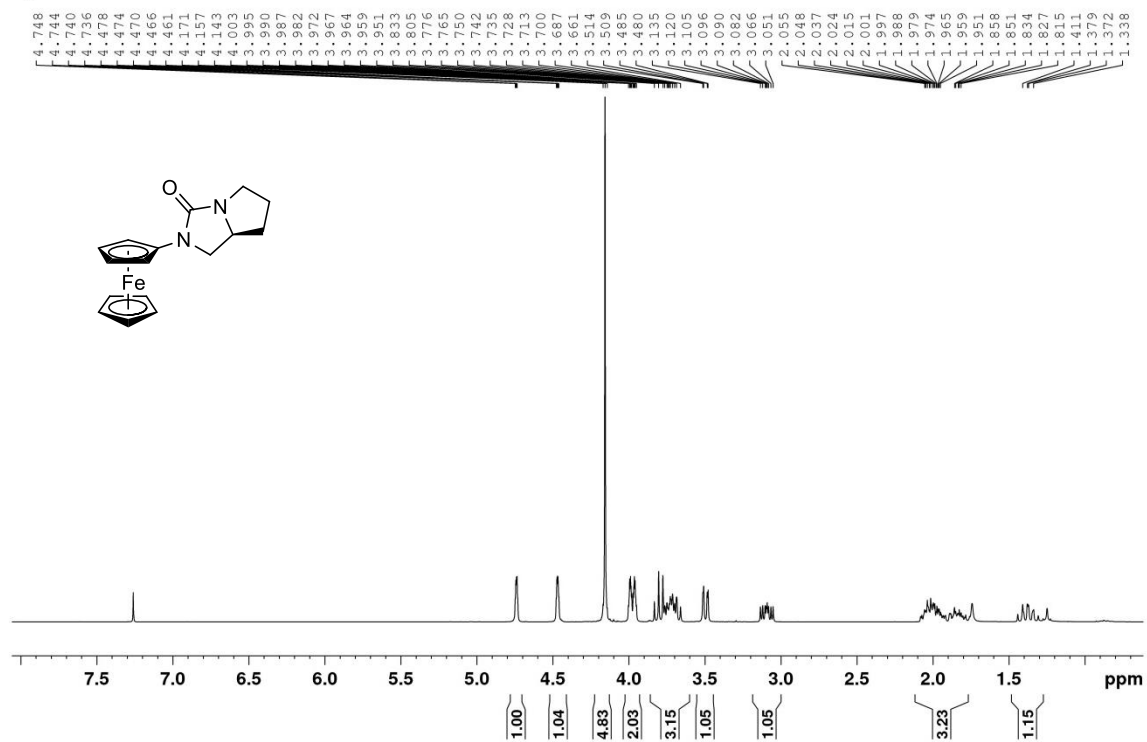


1D carbon with proton decoupling

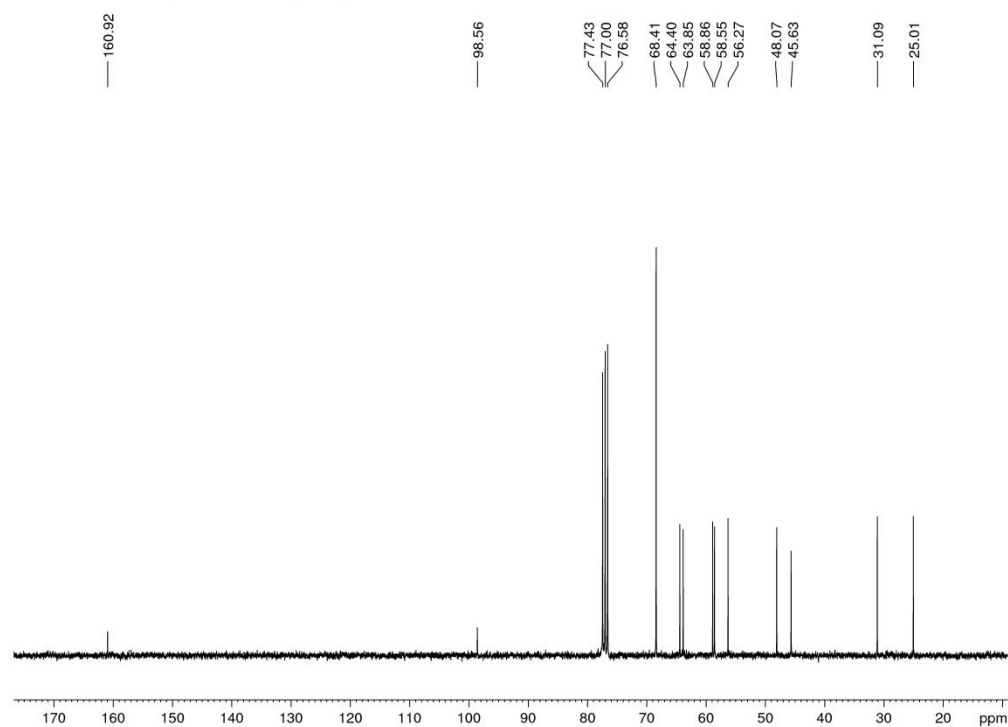


^1H and ^{13}C spectra for **230**.

1D proton

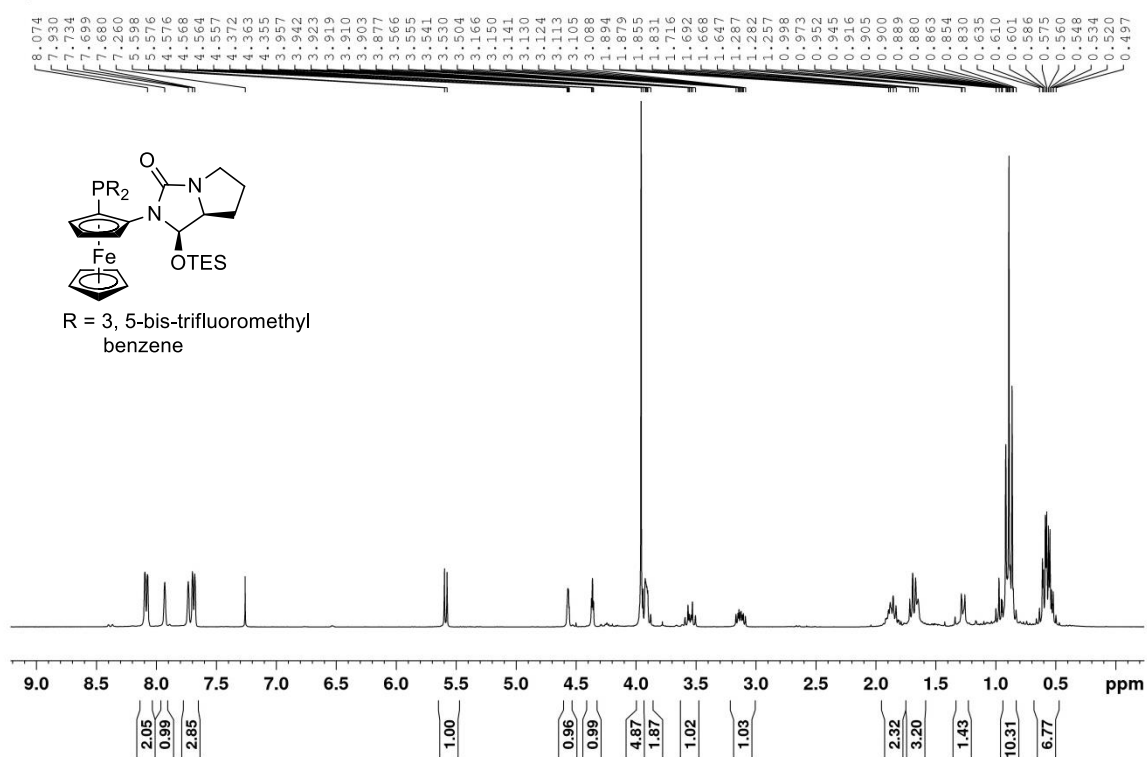


1D carbon with proton decoupling

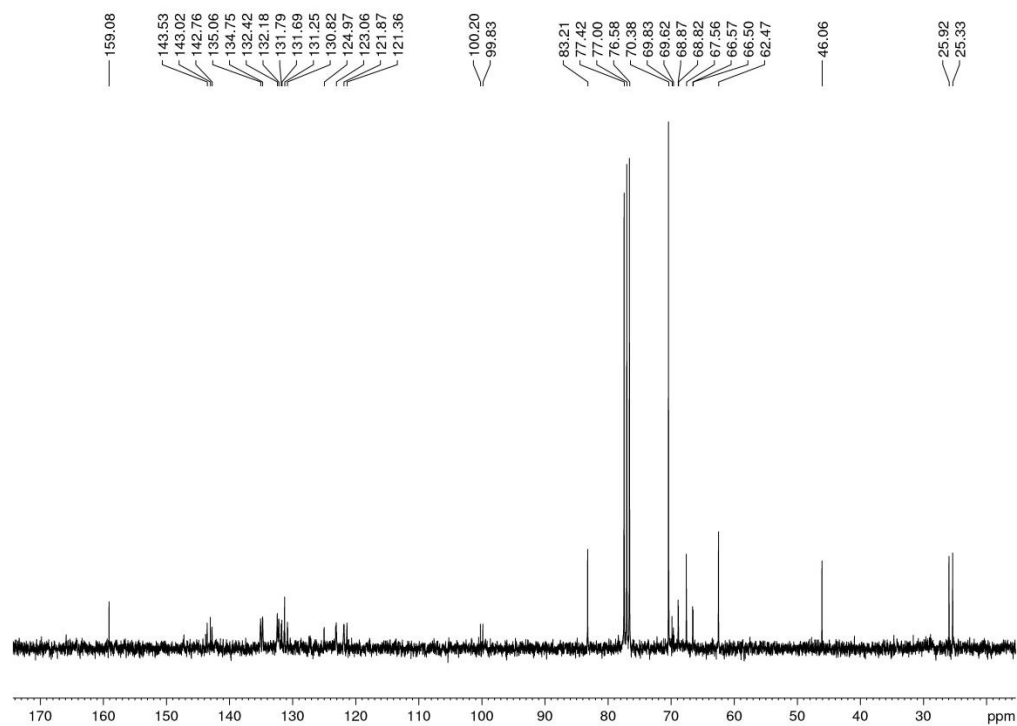


^1H and ^{13}C spectra for **229**.

1D proton

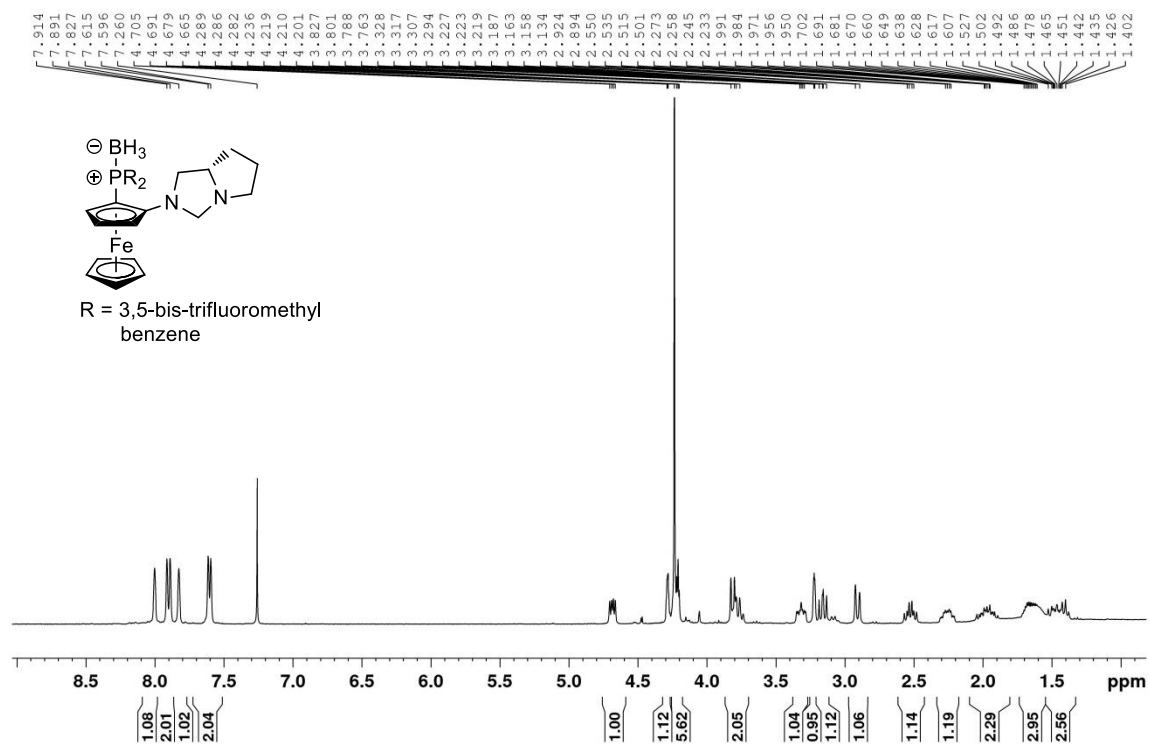


1D carbon with proton decoupling

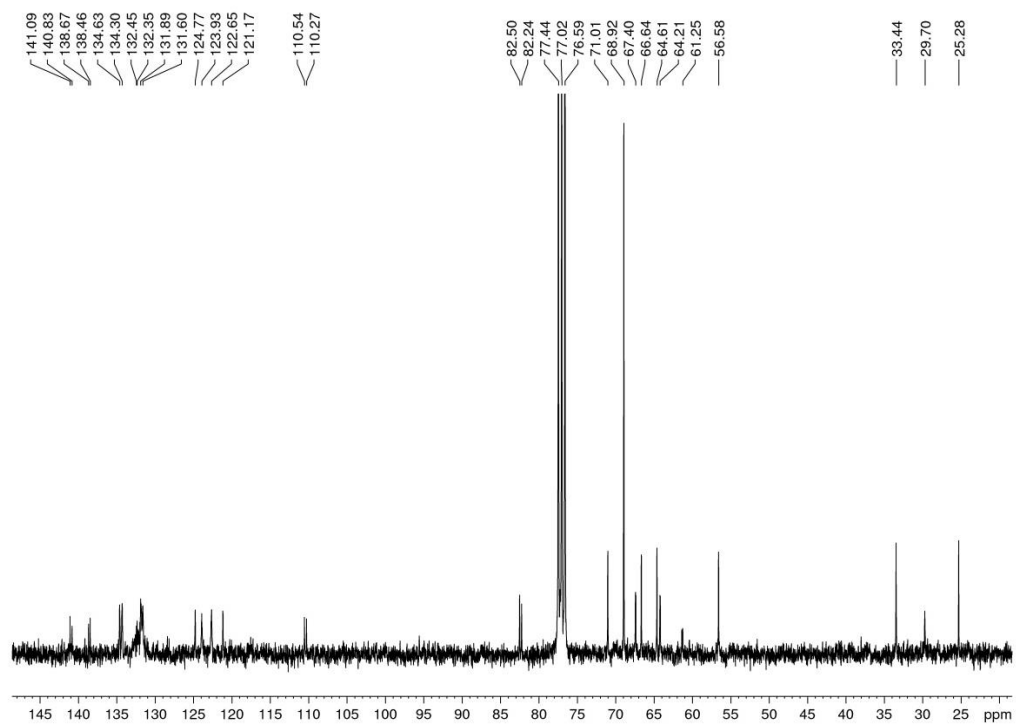


^1H and ^{13}C spectra for **231a**.

1D proton

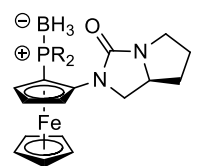
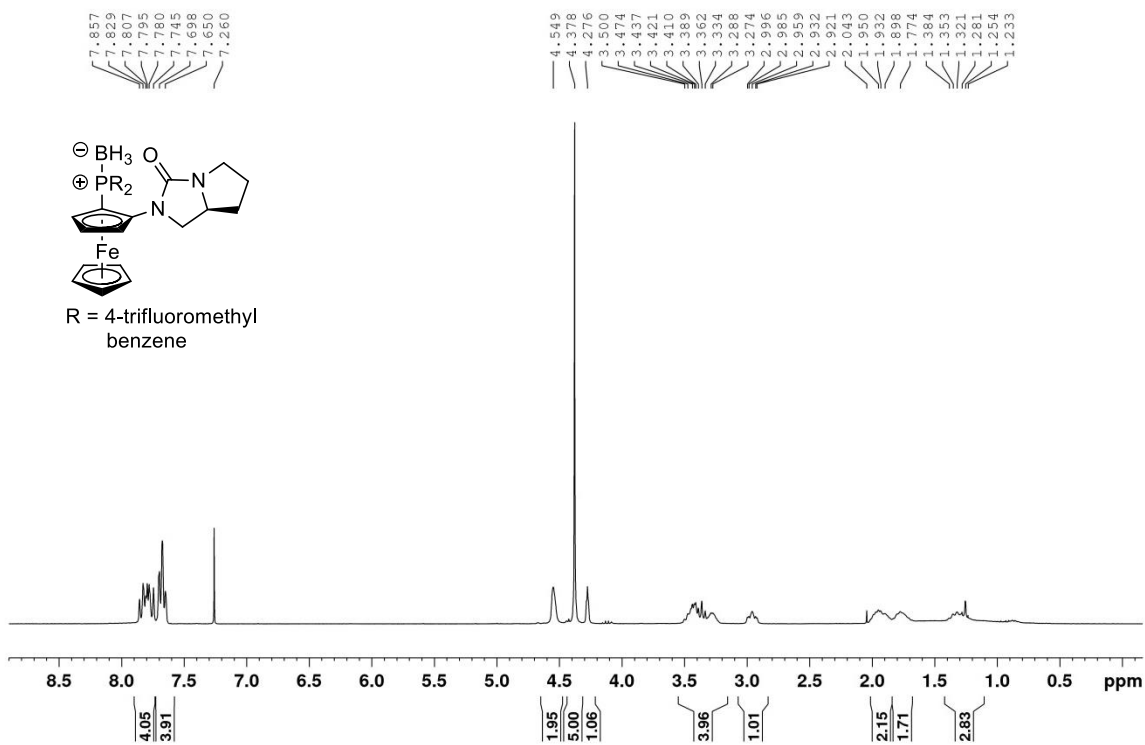


1D carbon with proton decoupling



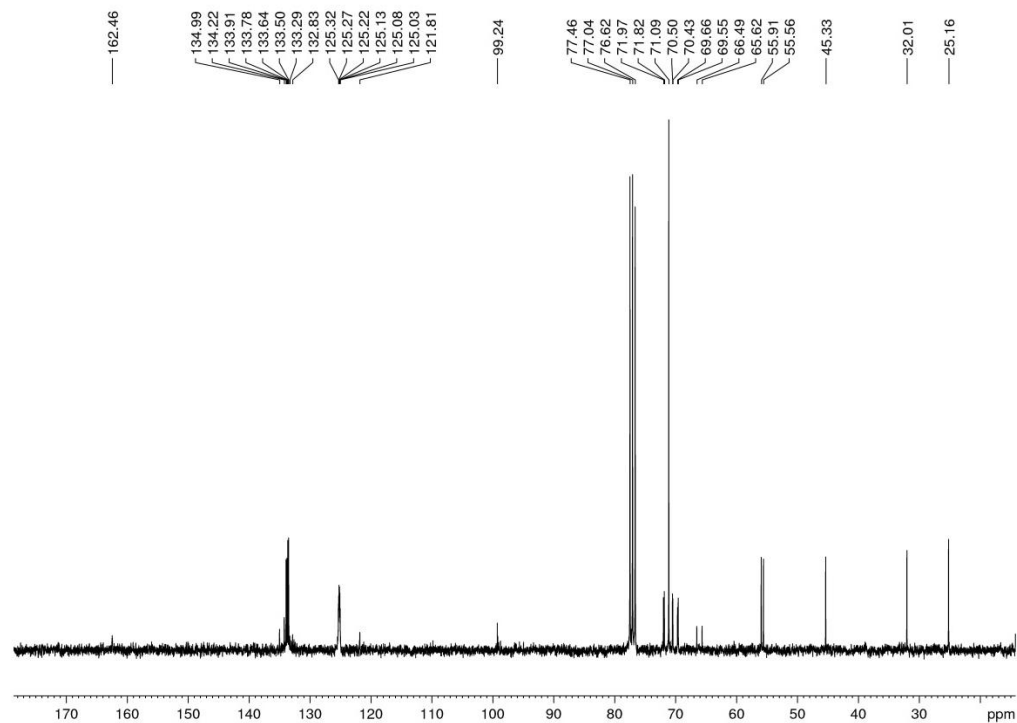
^1H and ^{13}C spectra for **232a**.

1D proton



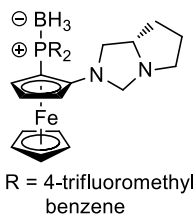
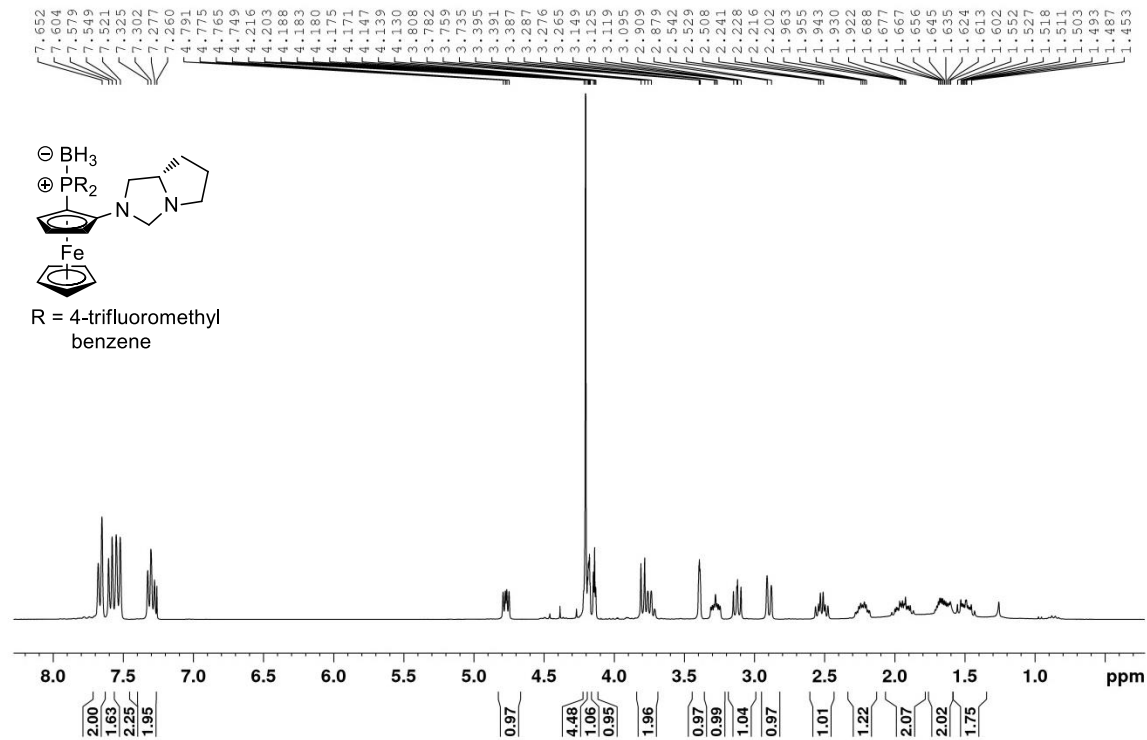
R = 4-trifluoromethyl benzene

1D carbon with proton decoupling

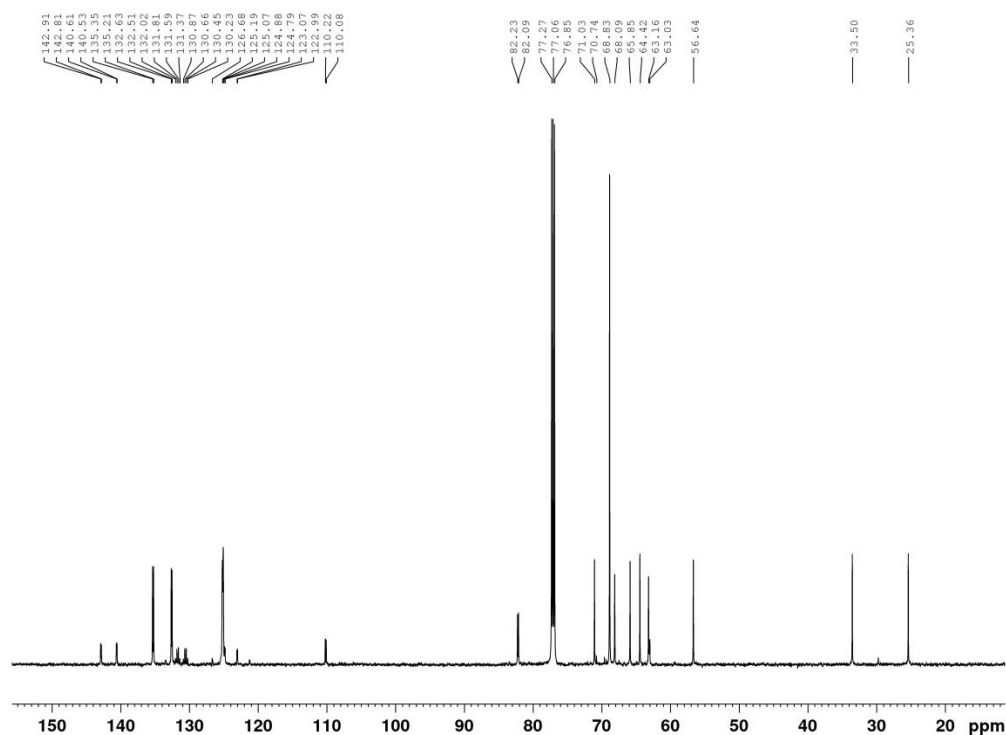


^1H and ^{13}C spectra for **232b**.

1D proton

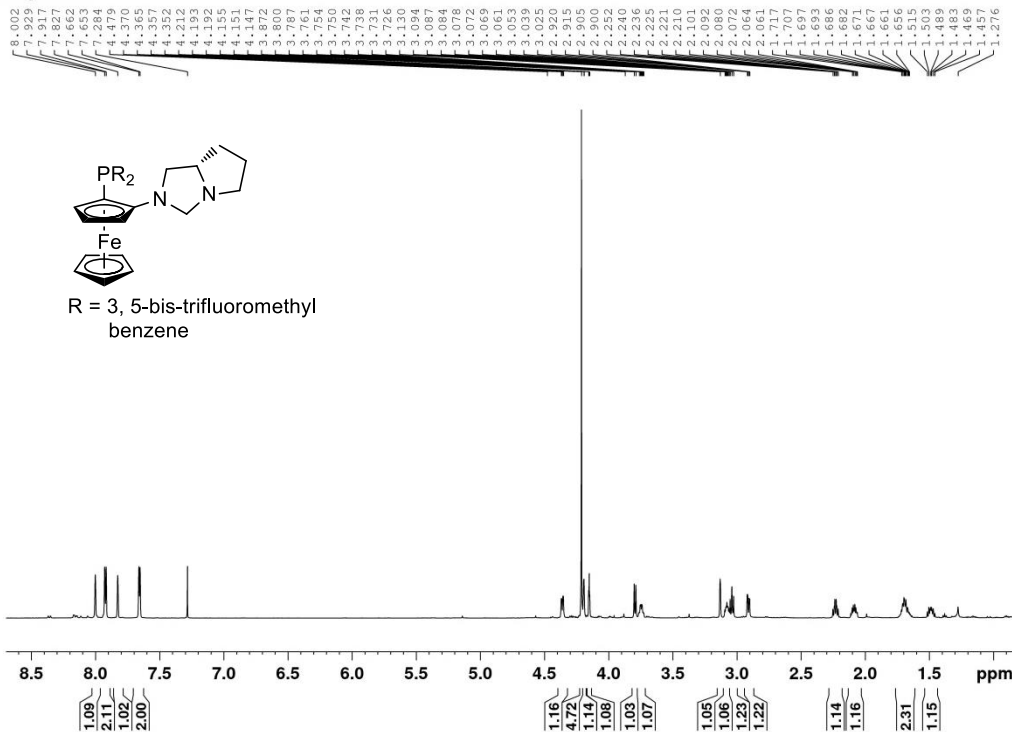


¹d carbon with proton decoupling

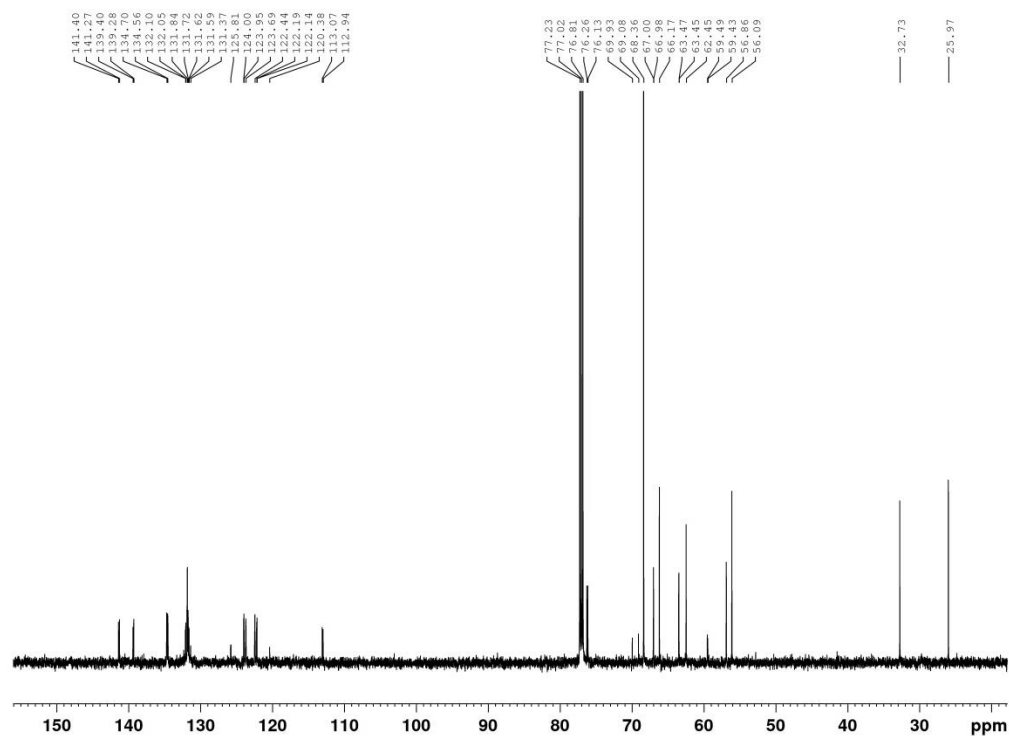


¹H and ¹³C spectra for **233b**.

¹d proton

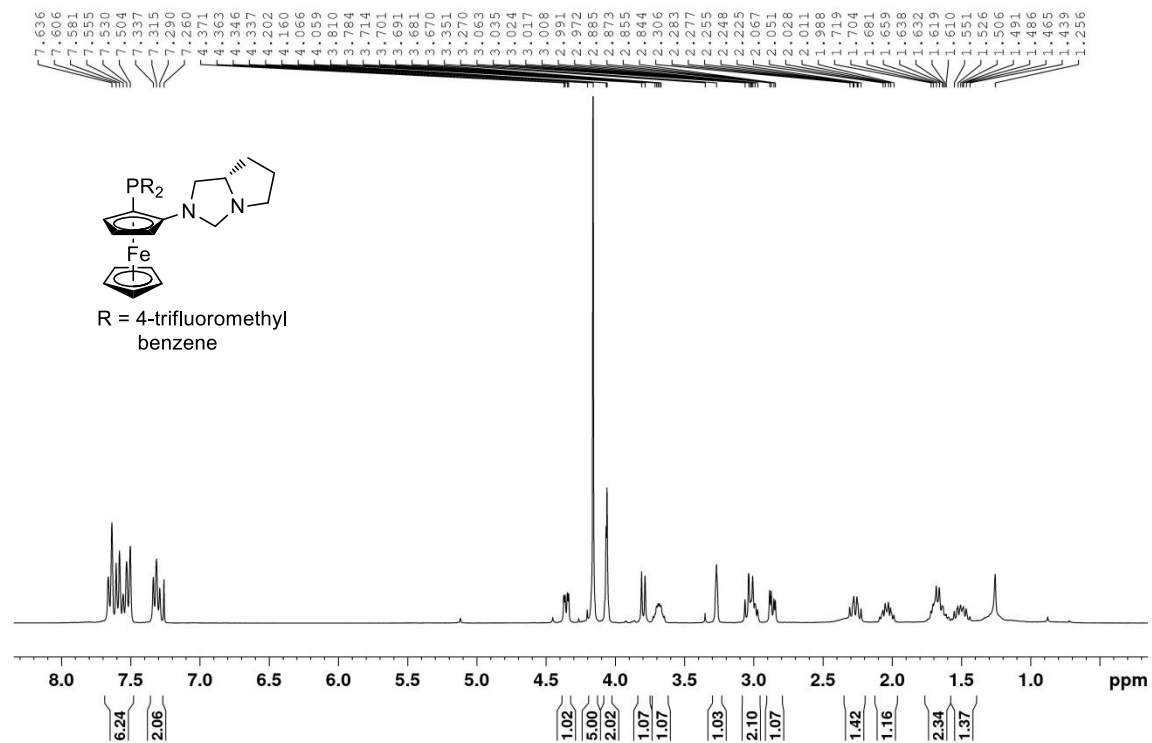


1d carbon with proton decoupling

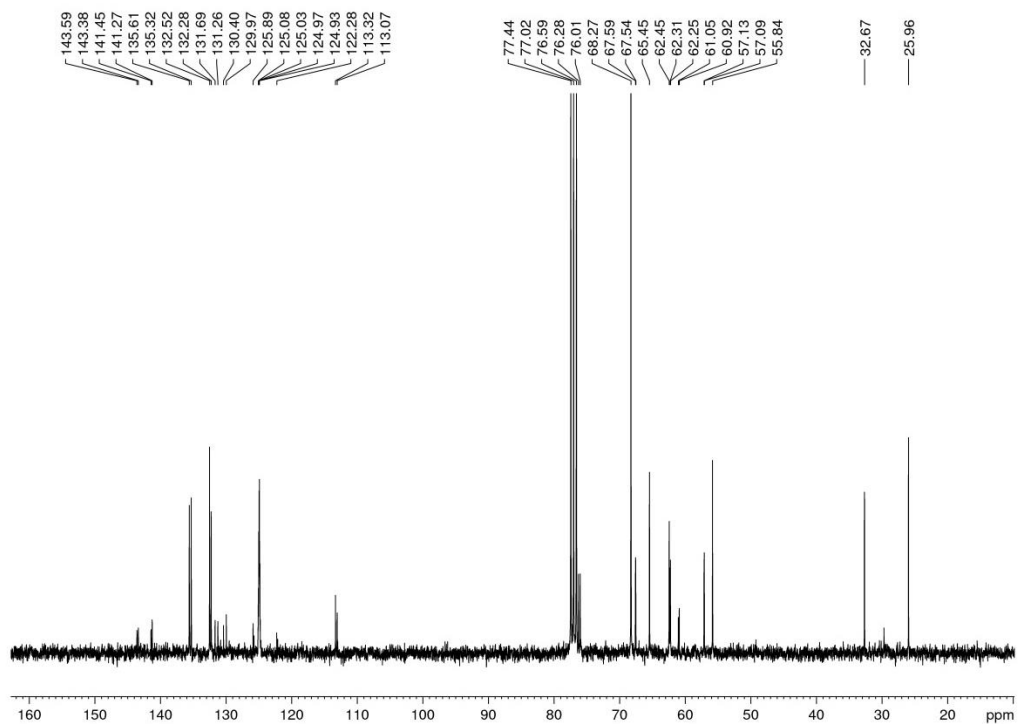


^1H and ^{13}C spectra for **234a**.

1D proton

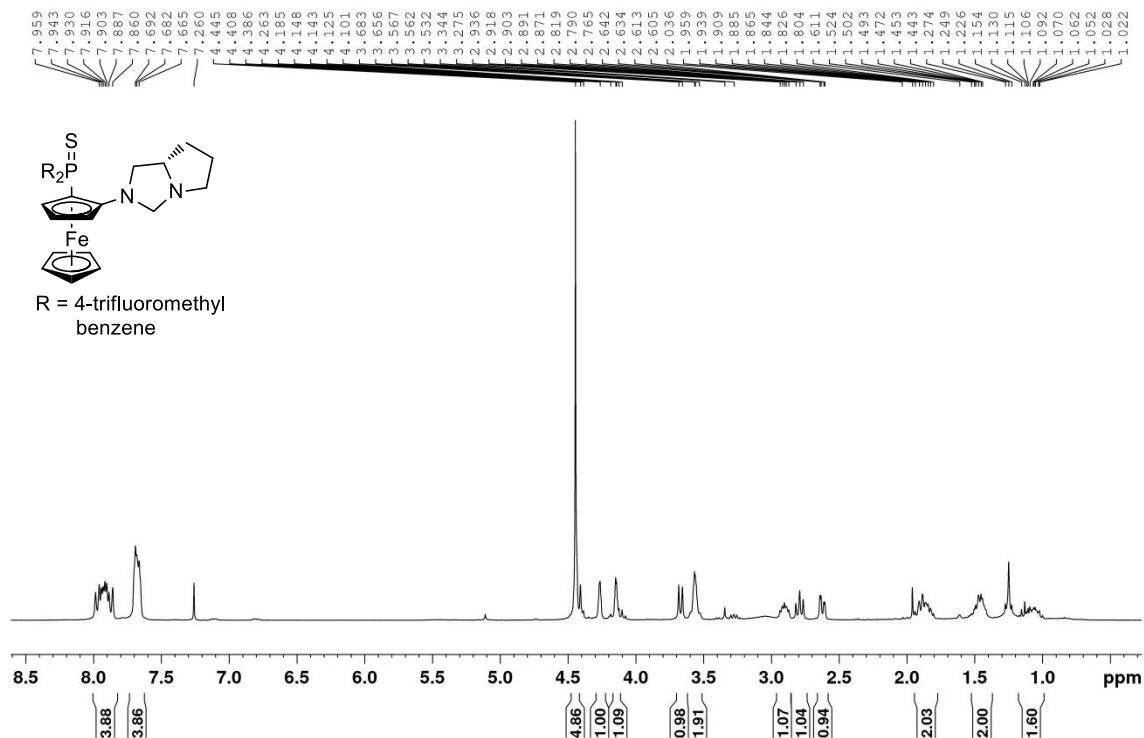


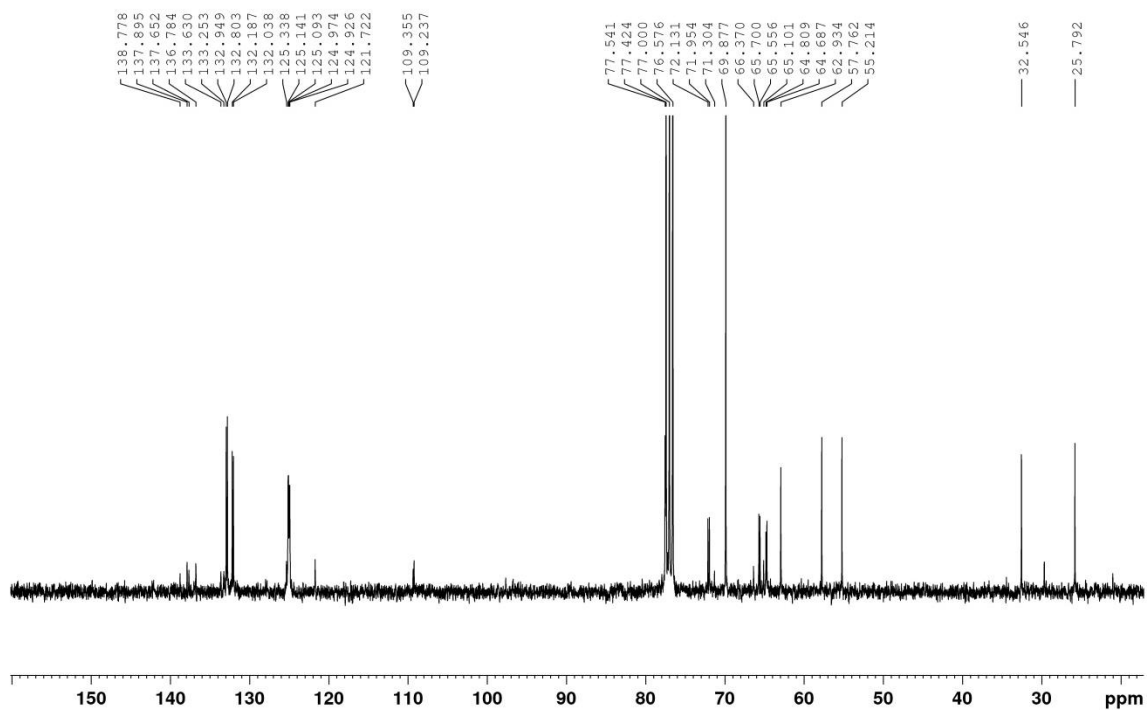
1D carbon with proton decoupling



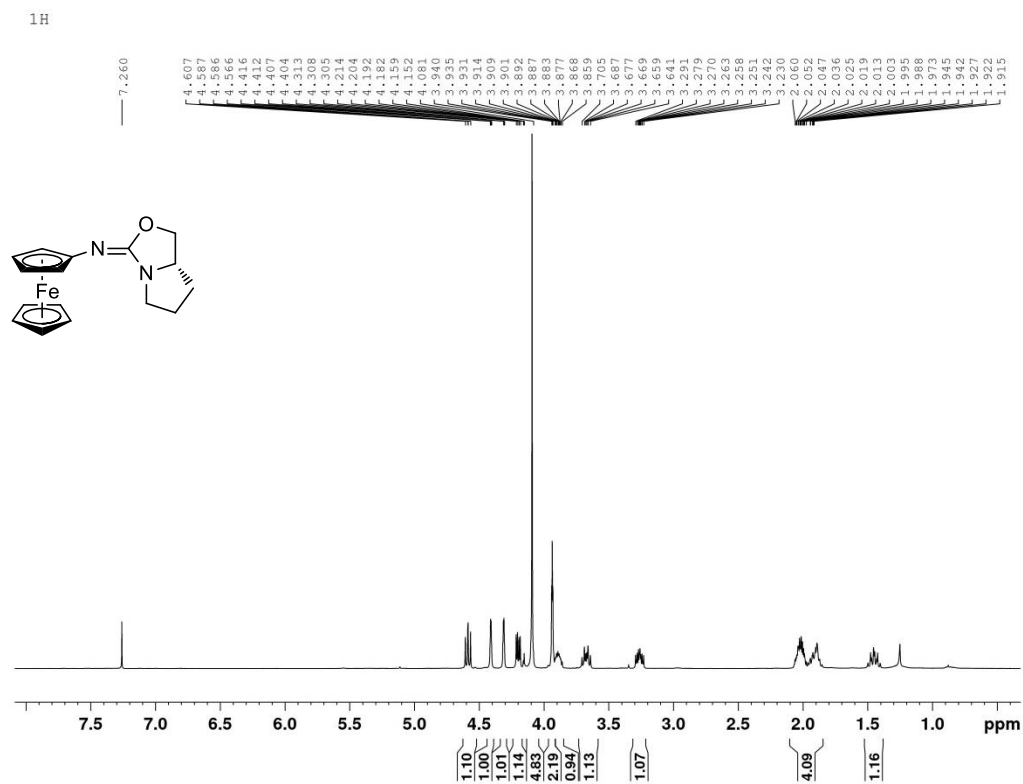
^1H and ^{13}C spectra for **234b**.

1D proton

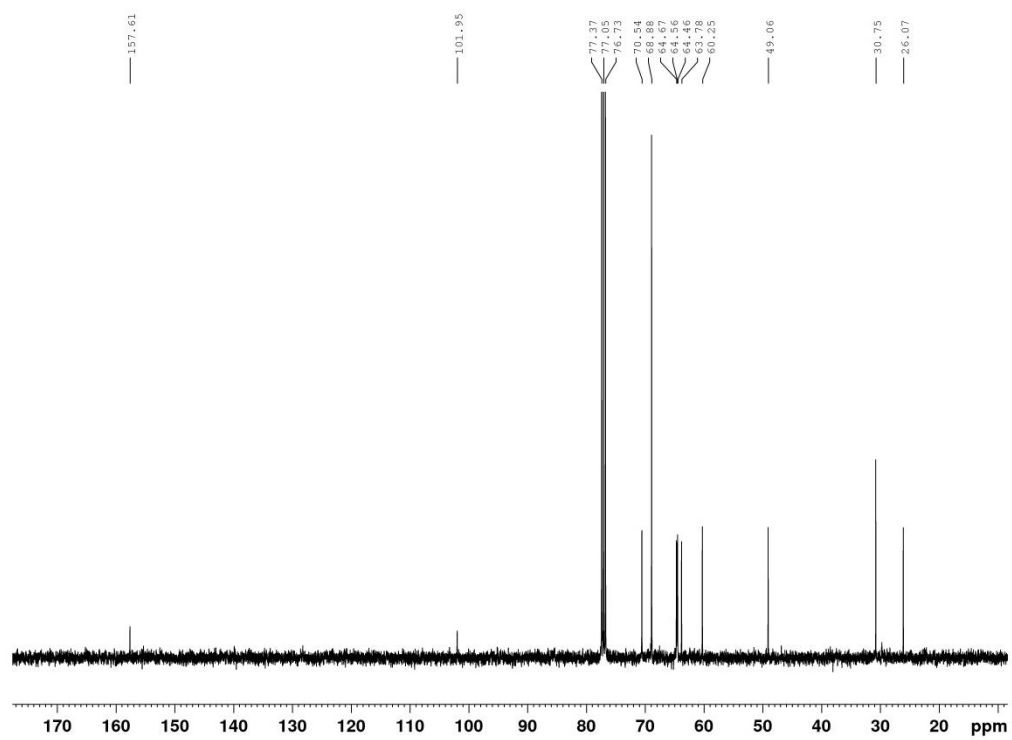




¹H and ¹³C spectra for **235**.



^{13}C with ^1H decoupling



^1H and ^{13}C spectra for **237**.

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